



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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|--|------------------------------|------------|---|----|------------|-----------------------------|----|------------|-----------------------------|----|------------|--------------------------|----|------------|--------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|-------------------------|----|------------|------------------------------|----|------------|------------------------------|----|------------|------------------------------|----|------------|------------------------------|----|------------|---------------------------|----|------------|---------------------------|----|------------|---------------------------|----|------------|---------------------------|----|------------|---------------------------|----|------------|----------------------------|----|--|
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| <p>(21) International Application Number: PCT/US99/23687</p> <p>(22) International Filing Date: 13 October 1999 (13.10.99)</p> <p>(30) Priority Data:</p> <table> <tbody> <tr><td>60/109,213</td><td>20 November 1998 (20.11.98)</td><td>US</td></tr> <tr><td>60/120,416</td><td>16 February 1999 (16.02.99)</td><td>US</td></tr> <tr><td>60/121,852</td><td>26 February 1999 (26.02.99)</td><td>US</td></tr> <tr><td>60/123,946</td><td>12 March 1999 (12.03.99)</td><td>US</td></tr> <tr><td>60/123,949</td><td>12 March 1999 (12.03.99)</td><td>US</td></tr> <tr><td>60/136,436</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/136,437</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/136,439</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/136,567</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/137,127</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/137,131</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/141,448</td><td>29 June 1999 (29.06.99)</td><td>US</td></tr> <tr><td>60/156,653</td><td>29 September 1999 (29.09.99)</td><td>US</td></tr> <tr><td>60/156,633</td><td>29 September 1999 (29.09.99)</td><td>US</td></tr> <tr><td>60/156,555</td><td>29 September 1999 (29.09.99)</td><td>US</td></tr> <tr><td>60/156,634</td><td>29 September 1999 (29.09.99)</td><td>US</td></tr> <tr><td>60/157,280</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>60/157,294</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>60/157,281</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>60/157,293</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>60/157,282</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>09/417,044</td><td>12 October 1999 (12.10.99)</td><td>US</td></tr> </tbody> </table> |                              | 60/109,213 | 20 November 1998 (20.11.98)   | US | 60/120,416 | 16 February 1999 (16.02.99) | US | 60/121,852 | 26 February 1999 (26.02.99) | US | 60/123,946 | 12 March 1999 (12.03.99) | US | 60/123,949 | 12 March 1999 (12.03.99) | US | 60/136,436 | 28 May 1999 (28.05.99) | US | 60/136,437 | 28 May 1999 (28.05.99) | US | 60/136,439 | 28 May 1999 (28.05.99) | US | 60/136,567 | 28 May 1999 (28.05.99) | US | 60/137,127 | 28 May 1999 (28.05.99) | US | 60/137,131 | 28 May 1999 (28.05.99) | US | 60/141,448 | 29 June 1999 (29.06.99) | US | 60/156,653 | 29 September 1999 (29.09.99) | US | 60/156,633 | 29 September 1999 (29.09.99) | US | 60/156,555 | 29 September 1999 (29.09.99) | US | 60/156,634 | 29 September 1999 (29.09.99) | US | 60/157,280 | 1 October 1999 (01.10.99) | US | 60/157,294 | 1 October 1999 (01.10.99) | US | 60/157,281 | 1 October 1999 (01.10.99) | US | 60/157,293 | 1 October 1999 (01.10.99) | US | 60/157,282 | 1 October 1999 (01.10.99) | US | 09/417,044 | 12 October 1999 (12.10.99) | US | 09/416,760<br><br>12 October 1999 (12.10.99)<br>US |
| 60/109,213   | 20 November 1998 (20.11.98)  | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/120,416   | 16 February 1999 (16.02.99)  | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
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| 60/123,946   | 12 March 1999 (12.03.99)     | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/123,949   | 12 March 1999 (12.03.99)     | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/136,436   | 28 May 1999 (28.05.99)       | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/136,437   | 28 May 1999 (28.05.99)       | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/136,439   | 28 May 1999 (28.05.99)       | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/136,567   | 28 May 1999 (28.05.99)       | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/137,127   | 28 May 1999 (28.05.99)       | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
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| 60/141,448   | 29 June 1999 (29.06.99)      | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/156,653   | 29 September 1999 (29.09.99) | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/156,633   | 29 September 1999 (29.09.99) | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/156,555   | 29 September 1999 (29.09.99) | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/156,634   | 29 September 1999 (29.09.99) | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/157,280   | 1 October 1999 (01.10.99)    | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/157,294   | 1 October 1999 (01.10.99)    | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| 60/157,281   | 1 October 1999 (01.10.99)    | US         |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
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|  |                              |            | (71) Applicant (for all designated States except US): ARENA PHARMACEUTICALS, INC. [US/US]; 6166 Nancy Ridge Drive, San Diego, CA 92121 (US).  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
|  |                              |            | (72) Inventors; and<br>(75) Inventors/Applicants (for US only): CHEN, Ruoping [CN/US]; 5296 Timber Branch Way, San Diego, CA 92130 (US). DANG, Huong, T. [US/US]; 5352 Oak Park Drive, San Diego, CA 92105 (US). LIAW, Chen, W. [US/US]; 7668 Salix Place, San Diego, CA 92129 (US). LIN, J-Lin [-/US]; 8291-7 Gold Coast Drive, San Diego, CA 92126 (US).  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
|  |                              |            | (74) Agents: MILLER, Suzanne, E. et al.; Woodcock Washburn Kurtz Mackiewicz & Norris LLP, 46th floor, One Liberty Place, Philadelphia, PA 19103 (US).   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
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| (54) Title: HUMAN ORPHAN G PROTEIN-COUPLED RECEPTORS   |                              |            |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| (57) Abstract  |                              |            |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |
| <p>The invention disclosed in this patent document relates to transmembrane receptors, more particularly to endogenous, human orphan G protein-coupled receptors.</p>  |                              |            |   |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |  |

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| CG | Congo                    | KE | Kenya                                    | NO | Norway                                       | YU | Yugoslavia               |
| CH | Switzerland              | KG | Kyrgyzstan                               | NZ | New Zealand                                  | ZW | Zimbabwe                 |
| CI | Côte d'Ivoire            | KD | Democratic People's<br>Republic of Korea | PL | Poland                                       |    |                          |
| CM | Cameroon                 | KR | Republic of Korea                        | PT | Portugal                                     |    |                          |
| CN | China                    | KZ | Kazakhstan                               | RO | Romania                                      |    |                          |
| CU | Cuba                     | LC | Saint Lucia                              | RU | Russian Federation                           |    |                          |
| CZ | Czech Republic           | LI | Liechtenstein                            | SD | Sudan  |    |                          |
| DE | Germany                  | LK | Sri Lanka                                | SE | Sweden                                       |    |                          |
| DK | Denmark                  | LR | Liberia                                  | SG | Singapore                                    |    |                          |

**HUMAN ORPHAN G PROTEIN-COUPLED RECEPTORS**

This patent document claims priority benefit of each of the following applications, all filed with the United States Patent and Trademark Office via U.S. Express Mail on the indicated filing dates: U.S. Provisional Number 60/121,852, filed; February 26, 1999 claiming the benefit of U.S. Provisional Number 60/109,213, filed November 20, 1998; U.S. Provisional Number 60/120,416, filed February 16, 1999; U.S. Provisional Number 60/123,946, filed March 12, 1999; U.S. Provisional Number 60/123,949, filed March 12, 1999; U.S. Provisional Number 60/136,436, filed May 28, 1999; U.S. Provisional Number 60/136,439, filed May 28, 1999; U.S. Provisional Number 60/136,567, filed May 28, 1999; U.S. Provisional Number 60/137,127, filed May 28, 1999; U.S. Provisional Number 60/137,131, filed May 28, 1999; U.S. Provisional Number 141,448, filed June 29, 1999 claiming priority from U.S. Provisional Number 60/136,437, filed May 28, 1999; U.S. Provisional Number \_\_\_\_\_ (Arena Pharmaceuticals, Inc. docket number 15 CHN10-1), filed September 29, 1999; U.S. Provisional Number 60/156,333, filed September 29, 1999; U.S. Provisional Number 60/156,555, filed September 29, 1999; U.S. Provisional Number 60/156,634, filed September 29, 1999; U.S. Provisional Number \_\_\_\_\_ (Arena Pharmaceuticals, Inc. docket number RUP6-1), filed October 1, 1999; U.S. Provisional Number \_\_\_\_\_ (Arena Pharmaceuticals, Inc. docket number RUP7-1), filed October 1, 1999; U.S. Provisional Number \_\_\_\_\_ (Arena Pharmaceuticals, Inc. docket number CHN6-1), filed October 1, 1999; U.S. Provisional

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Number \_\_\_\_\_ (Arena Pharmaceuticals, Inc. docket number RUP5-1), filed October 1, 1999; U.S. Provisional Number \_\_\_\_\_ (Arena Pharmaceuticals, Inc. docket number CHN9-1), filed October 1, 1999. This patent document is related to U.S. Serial Number 09/170,496 filed October 13, 1998, and U.S. Serial Number unknown (Woodcock & Washburn Kurtz Mackiewicz & Norris, LLP docket number AREN-0054 ) filed on October 12, 1999 (via U.S. Express Mail) both being incorporated herein by reference. This patent document also is related to U.S. Serial No. 09/364,425; filed July 30, 1999, which is incorporated by reference in its entirety. This application also claims priority to U.S. Serial Number \_\_\_\_\_ (Woodcock, Washburn, Kurtz, Makiewicz & Norris, LLP docket number AREN-0050), filed on October 12, 1999 (via U.S. Express Mail), incorporated by reference herein in its entirety. Each of the foregoing applications are incorporated herein by reference in their entirety.

### **FIELD OF THE INVENTION**

The invention disclosed in this patent document relates to transmembrane receptors, and more particularly to endogenous, orphan, human G protein-coupled receptors ("GPCRs").

### **BACKGROUND OF THE INVENTION**

Although a number of receptor classes exist in humans, by far the most abundant and therapeutically relevant is represented by the G protein-coupled receptor (GPCR or GPCRs) class. It is estimated that there are some 100,000 genes within the human genome, and of these, approximately 2% or 2,000 genes, are estimated to code for GPCRs. Receptors, including GPCRs, for which the endogenous ligand has been identified are referred to as "known" receptors, while receptors for which the endogenous ligand has not been identified

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are referred to as "orphan" receptors. GPCRs represent an important area for the development of pharmaceutical products: from approximately 20 of the 100 known GPCRs, 60% of all prescription pharmaceuticals have been developed. This distinction is not merely semantic, particularly in the case of GPCRs. Thus, the orphan GPCRs are to the pharmaceutical industry what gold was to California in the late 19<sup>th</sup> century – an opportunity to drive growth, expansion, enhancement and development.

5 GPCRs share a common structural motif. All these receptors have seven sequences of between 22 to 24 hydrophobic amino acids that form seven alpha helices, each of which spans the membrane (each span is identified by number, *i.e.*, transmembrane-1 (TM-1),  
10 transmebrane-2 (TM-2), etc.). The transmembrane helices are joined by strands of amino acids between transmembrane-2 and transmembrane-3, transmembrane-4 and transmembrane-5, and transmembrane-6 and transmembrane-7 on the exterior, or  
15 "extracellular" side, of the cell membrane (these are referred to as "extracellular" regions 1, 2 and 3 (EC-1, EC-2 and EC-3), respectively). The transmcmbbrane helices are also joined by strands of amino acids between transmembrane-1 and transmembrane-2, transmembrane-3 and transmembrane-4, and transmembrane-5 and transmembrane-6 on the interior, or  
20 "intracellular" side, of the cell membrane (these are referred to as "intracellular" regions 1, 2 and 3 (IC-1, IC-2 and IC-3), respectively). The "carboxy" ("C") terminus of the receptor lies in the intracellular space within the cell, and the "amino" ("N") terminus of the receptor lies in the extracellular space outside of the cell.

Generally, when an endogenous ligand binds with the receptor (often referred to as "activation" of the receptor), there is a change in the conformation of the intracellular region that allows for coupling between the intracellular region and an intracellular "G-protein." It

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has been reported that GPCRs are "promiscuous" with respect to G proteins, i.e., that a GPCR can interact with more than one G protein. See, Kenakin, T., 43 *Life Sciences* 1095 (1988). Although other G proteins exist, currently, Gq, Gs, Gi, and Go are G proteins that have been identified. Endogenous ligand-activated GPCR coupling with the G-protein begins a signaling cascade process (referred to as "signal transduction"). Under normal conditions, signal transduction ultimately results in cellular activation or cellular inhibition. It is thought that the IC-3 loop as well as the carboxy terminus of the receptor interact with the G protein.

Under physiological conditions, GPCRs exist in the cell membrane in equilibrium between two different conformations: an "inactive" state and an "active" state. A receptor in an inactive state is unable to link to the intracellular signaling transduction pathway to produce a biological response. Changing the receptor conformation to the active state allows linkage to the transduction pathway (via the G-protein) and produces a biological response. A receptor may be stabilized in an active state by an endogenous ligand or a compound such as a drug.

## SUMMARY OF THE INVENTION

Disclosed herein are human endogenous orphan G protein-coupled receptors.

## BRIEF DESCRIPTION OF THE DRAWINGS

**Figures 1A and 1B** provide reference "grids" for certain dot-blots provided herein 20 (*see also*, Figure 2A and 2B, respectively).

**Figures 2A and 2B** provide reproductions of the results of certain dot-blot analyses resulting from hCHN3 and hCHN8, respectively (*see also*, Figures 1A and 1B, respectively).

**Figure 3** provides a reproduction of the results of RT-PCR analysis of hRUP3.

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**Figure 4** provides a reproduction of the results of RT-PCR analysis of hRUP4.

**Figure 5** provides a reproduction of the results of RT-PCR analysis of hRUP6.

### DETAILED DESCRIPTION

The scientific literature that has evolved around receptors has adopted a number of terms to refer to ligands having various effects on receptors. For clarity and consistency, the following definitions will be used throughout this patent document. To the extent that these definitions conflict with other definitions for these terms, the following definitions shall control:

**AMINO ACID ABBREVIATIONS** used herein are set out in Table 1:

|    | TABLE I       |     |
|----|---------------|-----|
|    | ALANINE       | ALA |
|    | ARGININE      | ARG |
|    | ASPARAGINE    | ASN |
|    | ASPARTIC ACID | ASP |
| 15 | CYSTEINE      | CYS |
|    | GLUTAMIC ACID | GLU |
|    | GLUTAMINE     | GLN |
|    | GLYCINE       | GLY |
|    | HISTIDINE     | HIS |
| 20 | ISOLEUCINE    | ILE |
|    | LEUCINE       | LEU |
|    | LYSINE        | LYS |
|    | METHIONINE    | MET |
|    | PHENYLALANINE | PHE |
| 25 | PROLINE       | PRO |
|    | SERINE        | SER |
|    | THREONINE     | THR |
|    | TRYPTOPHAN    | TRP |
|    | TYROSINE      | TYR |
| 30 | VALINE        | VAL |

**COMPOSITION** means a material comprising at least one component.

**ENDOGENOUS** shall mean a material that a mammal naturally produces.

**ENDOGENOUS** in reference to, for example and not limitation, the term "receptor," shall mean that which is naturally produced by a mammal (for example, and not limitation, a

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human) or a virus. By contrast, the term **NON-ENDOGENOUS** in this context shall mean that which is not naturally produced by a mammal (for example, and not limitation, a human) or a virus.

**HOST CELL** shall mean a cell capable of having a Plasmid and/or Vector incorporated therein. In the case of a prokaryotic Host Cell, a Plasmid is typically replicated as a autonomous molecule as the Host Cell replicates (generally, the Plasmid is thereafter isolated for introduction into a eukaryotic Host Cell); in the case of a eukaryotic Host Cell, a Plasmid is integrated into the cellular DNA of the Host Cell such that when the eukaryotic Host Cell replicates, the Plasmid replicates. Preferably, for the purposes of the invention disclosed herein, the Host Cell is eukaryotic, more preferably, mammalian, and most preferably selected from the group consisting of 293, 293T and COS-7 cells.

**LIGAND** shall mean an endogenous, naturally occurring molecule specific for an endogenous, naturally occurring receptor.

**NON-ORPHAN RECEPTOR** shall mean an endogenous naturally occurring molecule specific for an endogenous naturally occurring ligand wherein the binding of a ligand to a receptor activates an intracellular signaling pathway.

**ORPHAN RECEPTOR** shall mean an endogenous receptor for which the endogenous ligand specific for that receptor has not been identified or is not known.

**PLASMID** shall mean the combination of a Vector and cDNA. Generally, a Plasmid is introduced into a Host Cell for the purposes of replication and/or expression of the cDNA as a protein.

**VECTOR** in reference to cDNA shall mean a circular DNA capable of incorporating at least one cDNA and capable of incorporation into a Host Cell.

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The order of the following sections is set forth for presentational efficiency and is not intended, nor should be construed, as a limitation on the disclosure or the claims to follow.

### **Identification of Human GPCRs**

.5        The efforts of the Human Genome project have led to the identification of a plethora of information regarding nucleic acid sequences located within the human genome; it has been the case in this endeavor that genetic sequence information has been made available without an understanding or recognition as to whether or not any particular genomic sequence does or may contain open-reading frame information that translate human proteins.

10 Several methods of identifying nucleic acid sequences within the human genome are within the purview of those having ordinary skill in the art. For example, and not limitation, a variety of GPCRs, disclosed herein, were discovered by reviewing the GenBank™ database, while other GPCRs were discovered by utilizing a nucleic acid sequence of a GPCR, previously sequenced, to conduct a BLAST™ search of the EST database. **Table A**, below, 15 lists the disclosed endogenous orphan GPCRs along with a GPCR's respective homologous GPCR:

**TABLE A**

|    | <b>Disclosed</b> | <b>Accession</b>  | <b>Open Reading</b> | <b>Per Cent</b>      | <b>Reference To</b>    |
|----|------------------|-------------------|---------------------|----------------------|------------------------|
|    | <b>Human</b>     | <b>Number</b>     | <b>Frame</b>        | <b>Homology</b>      | <b>Homologous</b>      |
| 20 | <b>Orphan</b>    | <b>Identified</b> | <b>(Base Pairs)</b> | <b>To Designated</b> | <b>GPCR</b>            |
|    |                  |                   |                     |                      | <b>(Accession No.)</b> |
|    | <b>hARE-3</b>    | AL033379          | 1,260 bp            | 52.3% LPA-R          | U92642                 |
|    | <b>hARE-4</b>    | AC006087          | 1,119 bp            | 36% P2Y5             | AF000546               |

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|    |               |             |          |                      |           |
|----|---------------|-------------|----------|----------------------|-----------|
|    | <b>hARE-5</b> | AC006255    | 1,104 bp | 32% <i>Oryzias</i>   | D43633    |
|    | <b>hGPR27</b> | AA775870    | 1,128 bp | <i>latipes</i>       |           |
|    | <b>hARE-1</b> | AI090920    | 999 bp   | 43%                  | D13626    |
|    | <b>hARE-2</b> | AA359504    | 1,122 bp | KIAA0001             |           |
| 5  | <b>hPPR1</b>  | H67224      | 1,053 bp | 53% GPR27            |           |
|    | <b>hG2A</b>   | AA754702    | 1,113 bp | 39% EBI1             | L31581    |
|    | <b>hRUP3</b>  | AL035423    | 1,005 bp | 31% GPR4             | L36148    |
|    |               |             |          | 30%                  | 2133653   |
|    |               |             |          | <i>Drosophila</i>    |           |
|    | <b>hRUP4</b>  | AI307658    | 1,296 bp | <i>melanogaster</i>  |           |
|    |               |             |          | 32% pNPGPR           | NP_004876 |
|    |               |             |          | 28% and 29 %         | AAC41276  |
|    |               |             |          | <i>Zebra fish Ya</i> | and       |
|    |               |             |          | and Yb,              | AAB94616  |
|    | <b>hRUP5</b>  | AC005849    | 1,413 bp | respectively         |           |
|    |               |             |          | 25% DEZ              | Q99788    |
| 10 | <b>hRUP6</b>  | AC005871    | 1,245 bp | 23% FMLPR            | P21462    |
|    | <b>hRUP7</b>  | AC007922    | 1,173 bp | 48% GPR66            | NP_006047 |
|    | <b>hCHN3</b>  | EST 36581   | 1,113 bp | 43% H3R              | AF140538  |
|    | <b>hCHN4</b>  | AA804531    | 1,077 bp | 53% GPR27            |           |
| 15 | <b>hCHN6</b>  | EST 2134670 | 1,503 bp | 32% thrombin         | 4503637   |
|    | <b>hCHN8</b>  | EST 764455  | 1,029 bp | 36% edg-1            | NP_001391 |
|    |               |             |          | 47%                  | D13626    |
|    | <b>hCHN9</b>  | EST 1541536 | 1,077 bp | KIAA0001             |           |
|    | <b>hCHN10</b> | EST 1365839 | 1,055 bp | 41% LTB4R            | NM_000752 |
|    |               |             |          | 35% P2Y              | NM_002563 |

Receptor homology is useful in terms of gaining an appreciation of a role of the disclosed receptors within the human body. Additionally, such homology can provide insight 20 as to possible endogenous ligand(s) that may be natural activators for the disclosed orphan GPCRs.

#### B. Receptor Screening

Techniques have become more readily available over the past few years for

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endogenous-ligand identification (this, primarily, for the purpose of providing a means of conducting receptor-binding assays that require a receptor's endogenous ligand) because the traditional study of receptors has always proceeded from the a priori assumption (historically based) that the endogenous ligand must first be identified before discovery could proceed to 5 find antagonists and other molecules that could affect the receptor. Even in cases where an antagonist might have been known first, the search immediately extended to looking for the endogenous ligand. This mode of thinking has persisted in receptor research even after the discovery of constitutively activated receptors. What has not been heretofore recognized is that it is the active state of the receptor that is most useful for discovering agonists, partial 10 agonists, and inverse agonists of the receptor. For those diseases which result from an overly active receptor or an under-active receptor, what is desired in a therapeutic drug is a compound which acts to diminish the active state of a receptor or enhance the activity of the receptor, respectively, not necessarily a drug which is an antagonist to the endogenous ligand. This is because a compound that reduces or enhances the activity of the active receptor state 15 need not bind at the same site as the endogenous ligand. Thus, as taught by a method of this invention, any search for therapeutic compounds should start by screening compounds against the ligand-independent active state.

As is known in the art, GPCRs can be "active" in their endogenous state even without the binding of the receptor's endogenous ligand thereto. Such naturally-active receptors can 20 be screened for the direct identification (*i.e.*, without the need for the receptor's endogenous ligand) of, in particular, inverse agonists. Alternatively, the receptor can be "activated" via, *e.g.*, mutation of the receptor to establish a non-endogenous version of the receptor that is active in the absence of the receptor's endogenous ligand.

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Screening candidate compounds against an endogenous or non-endogenous, constitutively activated version of the human orphan GPCRs disclosed herein can provide for the direct identification of candidate compounds which act at this cell surface receptor, without requiring use of the receptor's endogenous ligand. By determining areas within 5 the body where the endogenous version of human GPCRs disclosed herein is expressed and/or over-expressed, it is possible to determine related disease/disorder states which are associated with the expression and/or over-expression of the receptor; such an approach is disclosed in this patent document.

With respect to creation of a mutation that may evidence constitutive activation of 10 human orphan GPCRs disclosed herein is based upon the distance from the proline residue at which is presumed to be located within TM6 of the GPCR typically nears the TM6/IC3 interface (such proline residue appears to be quite conserved). By mutating the amino acid residue located 16 amino acid residues from this residue (presumably located in the IC3 region of the receptor) to, most preferably, a lysine residue, such activation may be obtained. 15 Other amino acid residues may be useful in the mutation at this position to achieve this objective.

#### C. Disease/Disorder Identification and/or Selection

Preferably, the DNA sequence of the human orphan GPCR can be used to make a probe for (a) dot-blot analysis against tissue-mRNA, and/or (b) RT-PCR identification of 20 the expression of the receptor in tissue samples. The presence of a receptor in a tissue source, or a diseased tissue, or the presence of the receptor at elevated concentrations in diseased tissue compared to a normal tissue, can be preferably utilized to identify a correlation with a treatment regimen, including but not limited to, a disease associated

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with that disease. Receptors can equally well be localized to regions of organs by this technique. Based on the known functions of the specific tissues to which the receptor is localized, the putative functional role of the receptor can be deduced.

#### D. Screening of Candidate Compounds

##### 5        1. Generic GPCR screening assay techniques

When a G protein receptor becomes constitutively active (i.e., active in the absence of endogenous ligand binding thereto), it binds to a G protein (e.g., Gq, Gs, Gi, Go) and stimulates the binding of GTP to the G protein. The G protein then acts as a GTPase and slowly hydrolyzes the GTP to GDP, whereby the receptor, under normal conditions, becomes 10 deactivated. However, constitutively activated receptors continue to exchange GDP to GTP.

A non-hydrolyzable analog of GTP, [<sup>35</sup>S]GTP $\gamma$ S, can be used to monitor enhanced binding to membranes which express constitutively activated receptors. It is reported that [<sup>35</sup>S]GTP $\gamma$ S can be used to monitor G protein coupling to membranes in the absence and presence of ligand. An example of this monitoring, among other examples well-known and 15 available to those in the art, was reported by Traynor and Nahorski in 1995. The preferred use of this assay system is for initial screening of candidate compounds because the system is generically applicable to all G protein-coupled receptors regardless of the particular G protein that interacts with the intracellular domain of the receptor.

##### 2. Specific GPCR screening assay techniques

20       Once candidate compounds are identified using the "generic" G protein-coupled receptor assay (i.e., an assay to select compounds that are agonists, partial agonists, or inverse agonists), further screening to confirm that the compounds have interacted at the receptor site is preferred. For example, a compound identified by the "generic" assay may not bind to the

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receptor, but may instead merely "uncouple" the G protein from the intracellular domain.

a. *Gs and Gi.*

Gs stimulates the enzyme adenylyl cyclase. Gi (and Go), on the other hand, inhibit this enzyme. Adenylyl cyclase catalyzes the conversion of ATP to cAMP; thus, 5 constitutively activated GPCRs that couple the Gs protein are associated with increased cellular levels of cAMP. On the other hand, constitutively activated GPCRs that couple the Gi (or Go) protein are associated with decreased cellular levels of cAMP. *See, generally,* "Indirect Mechanisms of Synaptic Transmission," Chpt. 8, From Neuron To Brain (3<sup>rd</sup> Ed.) Nichols, J.G. et al eds. Sinauer Associates, Inc. (1992). Thus, assays that detect cAMP can 10 be utilized to determine if a candidate compound is, *e.g.*, an inverse agonist to the receptor (*i.e.*, such a compound would decrease the levels of cAMP). A variety of approaches known in the art for measuring cAMP can be utilized; a most preferred approach relies upon the use of anti-cAMP antibodies in an ELISA-based format. Another type of assay that can be utilized is a whole cell second messenger reporter system assay. Promoters on genes drive 15 the expression of the proteins that a particular gene encodes. Cyclic AMP drives gene expression by promoting the binding of a cAMP-responsive DNA binding protein or transcription factor (CREB) which then binds to the promoter at specific sites called cAMP response elements and drives the expression of the gene. Reporter systems can be constructed which have a promoter containing multiple cAMP response elements before the reporter 20 gene, *e.g.*,  $\beta$ -galactosidase or luciferase. Thus, a constitutively activated Gs-linked receptor causes the accumulation of cAMP that then activates the gene and expression of the reporter protein. The reporter protein such as  $\beta$ -galactosidase or luciferase can then be detected using standard biochemical assays (Chen et al. 1995).

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***Go and Gq.***

Gq and Go are associated with activation of the enzyme phospholipase C, which in turn hydrolyzes the phospholipid PIP<sub>2</sub>, releasing two intracellular messengers: 5 diacycloglycerol (DAG) and inistol 1,4,5-triphosphate (IP<sub>3</sub>). Increased accumulation of IP<sub>3</sub> is associated with activation of Gq- and Go-associated receptors. See, generally, "Indirect Mechanisms of Synaptic Transmission," Chpt. 8, From Neuron To Brain (3<sup>rd</sup> Ed.) Nichols, J.G. et al eds. Sinauer Associates, Inc. (1992). Assays that detect IP<sub>3</sub> accumulation can be utilized to determine if a candidate compound is, e.g., an inverse agonist to a Gq- or Go- associated receptor (*i.e.*, such a compound would decrease the levels of IP<sub>3</sub>). Gq-associated receptors can also been examined using an AP1 reporter assay in that Gq-dependent phospholipase C causes activation of genes containing AP1 elements; thus, activated Gq-associated receptors will evidence an increase in the expression of such genes, whereby inverse agonists thereto will evidence a decrease in such expression, and agonists will 15 evidence an increase in such expression. Commercially available assays for such detection are available.

**3. GPCR Fusion Protein**

The use of an endogenous, constitutively activated orphan GPCR, or a non-endogenous, constitutively activated orphan GPCR, for screening of candidate compounds 20 for the direct identification of inverse agonists, agonists and partial agonists provides a unique challenge in that, by definition, the receptor is active even in the absence of an endogenous ligand bound thereto. Thus, it is often useful that an approach be utilized that can enhance the signal obtained by the activated receptor. A preferred approach is the use of a GPCR Fusion Protein.

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Generally, once it is determined that a GPCR is or has been constitutively activated, using the assay techniques set forth above (as well as others), it is possible to determine the predominant G protein that couples with the endogenous GPCR. Coupling of the G protein to the GPCR provides a signaling pathway that can be assessed. Because it is most preferred 5 that screening take place by use of a mammalian expression system, such a system will be expected to have endogenous G protein therein. Thus, by definition, in such a system, the constitutively activated orphan GPCR will continuously signal. In this regard, it is preferred that this signal be enhanced such that in the presence of, e.g., an inverse agonist to the receptor, it is more likely that it will be able to more readily differentiate, particularly in the 10 context of screening, between the receptor when it is contacted with the inverse agonist.

The GPCR Fusion Protein is intended to enhance the efficacy of G protein coupling with the GPCR. The GPCR Fusion Protein is preferred for screening with a non-endogenous, constitutively activated GPCR because such an approach increases the signal that is most preferably utilized in such screening techniques, although the GPCR Fusion 15 Protein can also be (and preferably is) used with an endogenous, constitutively activated GPCR. This is important in facilitating a significant "signal to noise" ratio; such a significant ratio is import preferred for the screening of candidate compounds as disclosed herein.

The construction of a construct useful for expression of a GPCR Fusion Protein is within the purview of those having ordinary skill in the art. Commercially available 20 expression vectors and systems offer a variety of approaches that can fit the particular needs of an investigator. The criteria of importance for such a GPCR Fusion Protein construct is that the GPCR sequence and the G protein sequence both be in-frame (preferably, the sequence for the GPCR is upstream of the G protein sequence) and that the "stop" codon of

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the GPCR must be deleted or replaced such that upon expression of the GPCR, the G protein can also be expressed. The GPCR can be linked directly to the G protein, or there can be spacer residues between the two (preferably, no more than about 12, although this number can be readily ascertained by one of ordinary skill in the art). We have a preference (based upon convenience) of use of a spacer in that some restriction sites that are not used will, effectively, upon expression, become a spacer. Most preferably, the G protein that couples to the GPCR will have been identified prior to the creation of the GPCR Fusion Protein construct. Because there are only a few G proteins that have been identified, it is preferred that a construct comprising the sequence of the G protein (*i.e.*, a universal G protein construct) be available for insertion of an endogenous GPCR sequence therein; this provides for efficiency in the context of large-scale screening of a variety of different endogenous GPCRs having different sequences.

#### E. Other Utility

Although a preferred use of the human orphan GPCRs disclosed herein may be for the direct identification of candidate compounds as inverse agonists, agonists or partial agonists (preferably for use as pharmaceutical agents), these versions of human GPCRs can also be utilized in research settings. For example, *in vitro* and *in vivo* systems incorporating GPCRs can be utilized to further elucidate and understand the roles these receptors play in the human condition, both normal and diseased, as well as understanding the role of constitutive activation as it applies to understanding the signaling cascade. The value in human orphan GPCRs is that its utility as a research tool is enhanced in that by determining the location(s) of such receptors within the body, the GPCRs can be used to understand the role of these receptors in the human body before the endogenous ligand therefor is identified.

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Other uses of the disclosed receptors will become apparent to those in the art based upon, *inter alia*, a review of this patent document.

## EXAMPLES

The following examples are presented for purposes of elucidation, and not limitation, 5 of the present invention. While specific nucleic acid and amino acid sequences are disclosed herein, those of ordinary skill in the art are credited with the ability to make minor modifications to these sequences while achieving the same or substantially similar results reported below. Unless otherwise indicated below, all nucleic acid sequences for the disclosed endogenous orphan human GPCRs have been sequenced and verified. For 10 purposes of equivalent receptors, those of ordinary skill in the art will readily appreciate that conservative substitutions can be made to the disclosed sequences to obtain a functionally equivalent receptor.

### **Example 1 ENDOGENOUS HUMAN GPCRS**

#### **15 1. Identification of Human GPCRs**

Several of the disclosed endogenous human GPCRs were identified based upon a review of the GenBank database information. While searching the database, the following cDNA clones were identified as evidenced below.

|    | Disclosed | Accession | Complete DNA | Open Reading | Nucleic Acid | Amino   |
|----|-----------|-----------|--------------|--------------|--------------|---------|
| 20 | Human     | Number    | Sequence     | Frame        | SEQ.ID       | Acid    |
|    | Orphan    |           | (Base Pairs) | (Base Pairs) | NO.          | SEQ.ID. |
|    | GPCRs     |           |              |              |              | NO.     |

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|   |               |          |            |          |    |    |
|---|---------------|----------|------------|----------|----|----|
|   | <b>hARE-3</b> | AL033379 | 111,389 bp | 1,260 bp | 1  | 2  |
|   | <b>hARE-4</b> | AC006087 | 226,925 bp | 1,119 bp | 3  | 4  |
|   | <b>hARE-5</b> | AC006255 | 127,605 bp | 1,104 bp | 5  | 6  |
|   | <b>hRUP3</b>  | AL035423 | 140,094 bp | 1,005 bp | 7  | 8  |
| 5 | <b>hRUP5</b>  | AC005849 | 169,144 bp | 1,413 bp | 9  | 10 |
|   | <b>hRUP6</b>  | AC005871 | 218,807 bp | 1,245 bp | 11 | 12 |
|   | <b>hRUP7</b>  | AC007922 | 158,858 bp | 1,173 bp | 13 | 14 |

Other disclosed endogenous human GPCRs were identified by conducting a BLAST search of EST database (dbest) using the following EST clones as query sequences. The 10 following EST clones identified were then used as a probe to screen a human genomic library.

|    | <b>Disclosed</b> | <b>Query</b>      | <b>EST Clone/</b>                  | <b>Open</b>         | <b>Nucleic Acid</b> | <b>Amino Acid</b> |
|----|------------------|-------------------|------------------------------------|---------------------|---------------------|-------------------|
|    | <b>Human</b>     | <b>(Sequence)</b> | <b>Accession No.</b>               | <b>Reading</b>      | <b>SEQ.ID.NO.</b>   | <b>SEQ.ID.NO.</b> |
|    | <b>Orphan</b>    |                   | <b>Identified</b>                  | <b>Frame</b>        |                     |                   |
| 15 | <b>GPCRs</b>     |                   |                                    | <b>(Base Pairs)</b> |                     |                   |
|    | <b>hGPCR27</b>   | Mouse             | AA775870                           | 1,125 bp            | 15                  | 16                |
|    | <b>hARE-1</b>    | GPCR27<br>TDAG    | 1689643                            | 999 bp              | 17                  | 18                |
|    | <b>hARE-2</b>    | GPCR27            | AJ090920<br>68530                  | 1,122 bp            | 19                  | 20                |
|    | <b>hPPR1</b>     | Bovine            | AA359504<br>238667                 | 1,053 bp            | 21                  | 22                |
| 20 | <b>hG2A</b>      | PPR1<br>Mouse     | H67224<br><i>See Example 2(a).</i> | 1,113 bp            | 23                  | 24                |
|    |                  | 1179426           | <i>below</i>                       |                     |                     |                   |

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|   |                                 |                 |                             |          |    |    |
|---|---------------------------------|-----------------|-----------------------------|----------|----|----|
|   | <b>hCHN3</b>                    | N.A.            | EST 36581<br>(full length)  | 1,113 bp | 25 | 26 |
|   | <b>hCHN4</b>                    | TDAG            | 1184934                     | 1,077 bp | 27 | 28 |
|   | <b>hCHN6</b>                    | N.A.            | AA804531<br>EST 2134670     | 1,503 bp | 29 | 30 |
| 5 | <b>hCHN8</b>                    | KIAA0001        | EST 764455<br>(full length) | 1,029 bp | 31 | 32 |
|   | <b>hCHN 9</b>                   | 1365839         | EST 1541536                 | 1,077 bp | 33 | 34 |
|   | <b>hCHN10</b>                   | Mouse EST       | Human 1365839               | 1,005 bp | 35 | 36 |
|   | <b>hRUP4</b>                    | N.A.<br>1365839 | AI307658                    | 1,296 bp | 37 | 38 |
|   | <i>N.A. = "not applicable".</i> |                 |                             |          |    |    |

## 2. Full Length Cloning

### 10 a. hG2A (Seq. Id. Nos. 23 & 24)

Mouse EST clone 1179426 was used to obtain a human genomic clone containing all but three amino acid hG2A coding sequences. The 5'end of this coding sequence was obtained by using 5'RACE™, and the template for PCR was Clontech's Human Spleen Marathon-ready™ cDNA. The disclosed human G2A was amplified by PCR using the G2A 15 cDNA specific primers for the first and second round PCR as shown in SEQ.ID.NO.: 39 and SEQ.ID.NO.:40 as follows:

5'-CTGTGTACAGCAGTTCGCAGAGTG-3' (SEQ.ID.NO.: 39; 1<sup>st</sup> round PCR)

5'-GAGTGCCAGGCAGAGCAGGTAGAC-3' (SEQ.ID.NO.: 40; second round PCR).

PCR was performed using Advantage™ GC Polymerase Kit (Clontech; manufacturing 20 instructions will be followed), at 94°C for 30 sec followed by 5 cycles of 94 °C for 5 sec and 72 °C for 4 min; and 30 cycles of 94° for 5 sec and 70° for 4 min. An approximate 1.3 Kb PCR fragment was purified from agarose gel, digested with Hind III and Xba I and cloned into the expression vector pRC/CMV2 (Invitrogen). The cloned-insert was sequenced using the T7 Sequenase™ kit (USB Amersham; manufacturer instructions will be followed) and

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the sequence was compared with the presented sequence. Expression of the human G2A will be detected by probing an RNA dot blot (Clontech; manufacturer instructions will be followed) with the P<sup>32</sup>-labeled fragment.

**b. hCHN9 (Seq. Id. Nos. 33 & 34)**

Sequencing of the EST clone 1541536 indicated that hCHN9 is a partial cDNA clone having only an initiation codon; *i.e.*, the termination codon was missing. When hCHN9 was used to "blast" against the data base (nr), the 3' sequence of hCHN9 was 100% homologous to the 5' untranslated region of the leukotriene B4 receptor cDNA, which contained a termination codon in the frame with hCHN9 coding sequence. To determine whether the 5' untranslated region of LTB4R cDNA was the 3' sequence of hCHN9, PCR was performed using primers based upon the 5' sequence flanking the initiation codon found in hCHN9 and the 3' sequence around the termination codon found in the LTB4R 5' untranslated region. The 5' primer sequence utilized was as follows:

5'-CCCGAATTCTGCTTGCTCCCAGCTTGGCCC-3' (SEQ.ID.NO.: 41: sense) and

155'-TGTGGATCCTGCTGTCAAAGGTCCCATTCCGG-3' (SEQ.ID.NO.: 42: antisense).

PCR was performed using thymus cDNA as a template and rTth polymerase (Perkin Elmer) with the buffer system provided by the manufacturer, 0.25 uM of each primer, and 0.2 mM of each 4 nucleotides. The cycle condition was 30 cycles of 94°C for 1 min, 65°C for 1 min and 72 °C for 1 min and 10 sec. A 1.1kb fragment consistent with the predicted size was obtained from PCR. This PCR fragment was subcloned into pCMV (*see* below) and sequenced (*see*, SEQ.ID.NO.: 33).

**c. hRUP4 (Seq. Id. Nos. 37 & 38)**

The full length hRUP4 was cloned by RT-PCR with human brain cDNA (Clontech)

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as templates:

5'-TCACAAATGCTAGGTGTGGTC-3' (SEQ.ID.NO.: 43; sense) and

5'-TGCATAGACAATGGGATTACAG-3' (SEQ.ID.NO.: 44; antisense).

PCR was performed using TaqPlus™ Precision™ polymerase (Stratagene; manufacturing 5 instructions will be followed) by the following cycles: 94°C for 2 min; 94°C 30 sec; 55°C for 30 sec, 72°C for 45 sec, and 72°C for 10 min. Cycles 2 through 4 were repeated 30 times.

The PCR products were separated on a 1% agarose gel and a 500 bp PCR fragment was isolated and cloned into the pCRII-TOPO vector (Invitrogen) and sequenced using the 10 T7 DNA Sequenase™ kit (Amsham) and the SP6/T7 primers (Stratagene). Sequence analysis revealed that the PCR fragment was indeed an alternatively spliced form of AI307658 having a continuous open reading frame with similarity to other GPCRs. The completed sequence of this PCR fragment was as follows:

5'-TCACAAATGCTAGGTGTGGCTGGCTGGCAGTCATCGTAGGATCACCCATGTGGCAC  
15 GTGCAACAACCTTGAGATCAAATATGACTTCCTATATGAAAAGGAACACATCTGCTGCTTAGAA  
GAGTGGACCAGCCCTGTGCACCAGAAAGATCTACACCACCTTCATCCTTGTCATCCTCTTCC  
TGCCTCTTATGGTATGCTTATTCTGTACGTAAAATTGGTTATGAACTTGGATAAAGAAAAGA  
GTTGGGGATGGTTCAGTGCTCGAACATTATGGAAAAGAAATGCCAAAATAGCCAGGAAG  
AAGAAACGAGCTGTCATTATGATGGTGACAGTGGTGGCTCTTGTGTGCTGGCACCA  
20 TTCCATGTTGTCATATGATGATTGAATACAGTAATTTGAAAAGGAATATGATGATGTCACA  
ATCAAGATGATTTTGCTATCGTCAAATTATTGGATTTCCAATCTGTAATCCCATTG  
TCTATGCA-3' (SEQ.ID.NO.: 45)

Based on the above sequence, two sense oligonucleotide primer sets:

5'-CTGCTTAGAAGAGTGGACCAG-3' (SEQ.ID.NO.: 46; oligo 1),

25 5'-CTGTGCACCAGAAGATCTACAC-3' (SEQ.ID.NO.: 47; oligo 2)

and two antisense oligonucleotide primer sets:

5'-CAAGGATGAAGGTGGTGTAGA-3' (SEQ.ID.NO.: 48; oligo 3)

5'-GTGTAGATCTTCTGGTGCACAGG-3' (SEQ.ID.NO.: 49; oligo 4)

were used for 3'- and 5'-race PCR with a human brain Marathon-Ready™ cDNA (Clontech,

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Cat# 7400-1) as template, according to manufacturer's instructions. DNA fragments generated by the RACE PCR were cloned into the pCRII-TOPO™ vector (Invitrogen) and sequenced using the SP6/T7 primers (Stratagene) and some internal primers. The 3' RACE product contained a poly(A) tail and a completed open reading frame ending at a TAA stop 5 codon. The 5' RACE product contained an incomplete 5' end; *i.e.*, the ATG initiation codon was not present.

Based on the new 5' sequence, oligo 3 and the following primer:

5'-GCAATGCAGGTCACTAGTGAGC -3' (SEQ.ID.NO.: 50; oligo 5)

were used for the second round of 5' RACE PCR and the PCR products were analyzed as 10 above. A third round of 5' RACE PCR was carried out utilizing antisense primers:

5'-TGGAGCATGGTGACGGGAATGCAGAAG-3' (SEQ.ID.NO.: 51; oligo 6) and

5'-GTGATGAGCAGGTCACTGAGCGCCAAG-3' (SEQ.ID.NO.: 52; oligo 7).

The sequence of the 5' RACE PCR products revealed the presence of the initiation codon ATG, and further round of 5' RACE PCR did not generate any more 5' sequence. The 15 completed 5' sequence was confirmed by RT-PCR using sense primer

5'-GCAATGCAGGCCTAACATTAC-3' (SEQ.ID.NO.: 53; oligo 8)

and oligo 4 as primers and sequence analysis of the 650 bp PCR product generated from 20 human brain and heart cDNA templates (Clontech, Cat# 7404-1). The completed 3' sequence was confirmed by RT-PCR using oligo 2 and the following antisense primer:

5'-TTGGGTTACAATCTGAAGGGCA-3' (SEQ.ID.NO.: 54; oligo 9)

and sequence analysis of the 670 bp PCR product generated from human brain and heart cDNA templates (Clontech, Cat# 7404-1).

**d. hRUP5 (Seq. Id. Nos. 9 & 10)**

The full length hRUP5 was cloned by RT-PCR using a sense primer upstream from

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ATG, the initiation codon (SEQ.ID.NO.: 55), and an antisense primer containing TCA as the stop codon (SEQ.ID.NO.: 56), which had the following sequences:

5'-ACTCCGTGTCCAGCAGGACTCTG-3' (SEQ.ID.NO.: 55)

5'-TGCCTGTTCTGGACCCTCACGTG-3' (SEQ.ID.NO.: 56)

5 and human peripheral leukocyte cDNA (Clontech) as a template. Advantage cDNA polymerase (Clontech) was used for the amplification in a 50ul reaction by the following cycle with step 2 through step 4 repeated 30 times: 94°C for 30 sec; 94° for 15 sec; 69° for 40 sec; 72°C for 3 min; and 72°C fro 6 min. A 1.4kb PCR fragment was isolated and cloned with the pCRII-TOPO™ vector (Invitrogen) and completely sequenced using the T7 DNA 10 Sequenase™ kit (Amsham). See, SEQ.ID.NO.: 9.

**e. hRUP6 (Seq. Id. Nos. 11 & 12)**

The full length hRUP6 was cloned by RT-PCR using primers:

5'-CAGGCCTTGGATTTAATGTCAGGGATGG-3' (SEQ.ID.NO.: 57) and

5'-GGAGAGTCAGCTCTGAAAGAATTCAAGG-3' (SEQ.ID.NO.: 58);

15 and human thymus Marathon-Ready™ cDNA (Clontech) as a template. Advantage cDNA polymerase (Clontech, according to manufacturer's instructions) was used for the amplification in a 50ul reaction by the following cycle: 94°C for 30sec; 94°C for 5 sec; 66°C for 40sec; 72°C for 2.5 sec and 72°C for 7 min. Cycles 2 through 4 were repeated 30 times. A 1.3 Kb PCR fragment was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) 20 and completely sequenced (see, SEQ.ID.NO.: 11) using the ABI Big Dye Terminator™ kit (P.E. Biosystem).

**f. hRUP7 (Seq. Id. Nos. 13 & 14)**

The full length RUP7 was cloned by RT-PCR using primers:

5'-TGATGTGATGCCAGATACTAATAGCAC-3' (SEQ.ID.NO.: 59; sense) and

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5'-CCTGATTCA~~TTAGGTGAGATTGAGAC-3'~~ (SEQ.ID.NO.: 60; antisense) and human peripheral leukocyte cDNA (Clontech) as a template. Advantage™ cDNA polymerase (Clontech) was used for the amplification in a 50 ul reaction by the following cycle with step 2 to step 4 repeated 30 times: 94°C for 2 minutes; 94°C for 15 seconds; 60°C 5 for 20 seconds; 72°C for 2 minutes; 72°C for 10 minutes. A 1.25 Kb PCR fragment was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) and completely sequenced using the ABI Big Dye Terminator™ kit (P.E. Biosystem). See, SEQ.ID.NO.: 13.

**g. hARE-5 (Seq. Id. Nos. 5 & 6)**

The full length hARE-5 was cloned by PCR using the hARE5 specific primers 10 5'-CAGCGCAGGGTGAAGCCTGAGAGC-3' SEQ.ID.NO.: 69 (sense, 5' of initiation codon ATG) and 5'-GGCACCTGCTGTGACCTGTGCAGG-3' SEQ.ID.NO.:70 (antisense, 3' of stop codon TGA) and human genomic DNA as template. TaqPlus Precision™ DNA polymerase (Stratagene) was used for the amplification by the following cycle with step 2 to step 4 repeated 35 times: 96°C, 2 minutes; 96°C, 20 seconds; 58°C, 30 seconds; 72°C, 2 minutes; and 72°C, 10 minutes  
15 A 1.1 Kb PCR fragment of predicated size was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) and completely sequenced (SEQ.ID.NO.:5) using the T7 DNA Sequenase™ kit (Amsham).

**h. hARE-4 (Seq. Id. Nos.: 3 & 4)**

The full length hARE-4 was cloned by PCR using the hARE-4 specific primers 5'-20 CTGGTGTGCTCCATGGCATCCC-3' SEQ.ID.NO.:67 (sense, 5' of initiation codon ATG) and 5'-GTAAGCCTCCCAGAACGAGAGG-3' SEQ.ID.NO.: 68 (antisense, 3' of stop codon TGA) and human genomic DNA as template. Taq DNA polymerase (Stratagene) and 5% DMSO was used for the amplification by the following cycle with step 2 to step 3 repeated 35 times:

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94°C, 3 minutes; 94°C, 30 seconds; 59°C, 2 minutes; 72°C, 10 minutes

A 1.12 Kb PCR fragment of predicated size was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) and completely sequenced (SEQ.ID.NO.:3) using the T7 DNA Sequenase™ kit (Amsham).

5           i. hARE-3 (Seq.Id.Nos.: 1 & 2)

The full length hARE-3 was cloned by PCR using the hARE-3 specific primers 5'-  
gatcaagcttCCATCCTACTGAAACCATGGTC-3' SEQ.ID.NO.:65 (sense, lower case nucleotides  
represent Hind III overhang, ATG as initiation codon) and 5'-  
gatcagatctCAGTTCCAATATTCACACCACCGTC-3' SEQ.ID.NO.:66 (antisense, lower case  
10 nucleotides represent Xba I overhang, TCA as stop codon) and human genomic DNA as  
template. TaqPlus Precision™ DNA polymerase (Stratagene) was used for the amplification  
by the following cycle with step 2 to step 4 repeated 35 times: 94°C, 3 minutes; 94°C, 1  
minute; 55°C, 1 minute; 72°C, 2 minutes; 72°C, 10 minutes.

A 1.3 Kb PCR fragment of predicated size was isolated and digested with Hind III  
15 and Xba I, cloned into the pRC/CMV2 vector (Invitrogen) at the Hind III and Xba I sites and  
completely sequenced (SEQ.ID.NO.:1) using the T7 DNA Sequenase™ kit (Amsham).

j. hRUP3 (Seq. Id. Nos.:7 & 8)

The full length hRUP3 was cloned by PCR using the hRUP3 specific primers 5'-  
GTCCTGCCACTTCGAGACATGG-3' SEQ.ID.NO.:71 (sense, ATG as initiation codon) and 5'-  
20 GAAACTTCTCTGCCCTTACCGTC-3' SEQ.ID.NO.:72 (antisense, 3' of stop codon TAA) and  
human genomic DNA as template. TaqPlus Precision™ DNA polymerase (Stratagene) was  
used for the amplification by the following cycle with step 2 to step 4 repeated 35 times:  
94°C, 3 minutes; 94°C, 1 minute; 58°C, 1 minute; 72°C, 2 minutes; 72°C, 10 minutes

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A 1.0 Kb PCR fragment of predicated size was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) and completely sequenced (SEQ.ID.NO.: 7) using the T7 DNA sequenase kit (Amsham).

**Example 2**  
**5 RECEPTOR EXPRESSION**

Although a variety of cells are available to the art for the expression of proteins, it is most preferred that mammalian cells be utilized. The primary reason for this is predicated upon practicalities, *i.e.*, utilization of, *e.g.*, yeast cells for the expression of a GPCR, while possible, introduces into the protocol a non-mammalian cell which may not (indeed, in the case of yeast, does not) include the receptor-coupling, genetic-mechanism and secretary pathways that have evolved for mammalian systems – thus, results obtained in non-mammalian cells, while of potential use, are not as preferred as that obtained from mammalian cells. Of the mammalian cells, COS-7, 293 and 293T cells are particularly preferred, although the specific mammalian cell utilized can be predicated upon the particular needs of the artisan. The general procedure for expression of the disclosed GPCRs is as follows.

On day one,  $1 \times 10^7$  293T cells per 150mm plate were plated out. On day two, two reaction tubes will be prepared (the proportions to follow for each tube are per plate); tube A will be prepared by mixing 20 $\mu$ g DNA (*e.g.*, pCMV vector; pCMV vector with receptor cDNA, etc.) in 1.2ml serum free DMEM (Irvine Scientific, Irvine, CA); tube B will be prepared by mixing 120 $\mu$ l lipofectamine (Gibco BRL) in 1.2ml serum free DMEM. Tubes A and B are admixed by inversions (several times), followed by incubation at room temperature for 30-45min. The admixture can be referred to as the "transfection mixture". Plated 293T cells are washed with 1XPBS, followed by addition of 10ml serum free DMEM.

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2.4ml of the transfection mixture will then be added to the cells, followed by incubation for 4hrs at 37°C/5% CO<sub>2</sub>. The transfection mixture was then be removed by aspiration, followed by the addition of 25ml of DMEM/10% Fetal Bovine Serum. Cells will then be incubated at 37°C/5% CO<sub>2</sub>. After 72hr incubation, cells can then be harvested and utilized for analysis.

### 5 Example 3

#### TISSUE DISTRIBUTION OF THE DISCLOSED HUMAN GPCRS

Several approaches can be used for determination of the tissue distribution of the GPCRs disclosed herein.

##### 1. Dot-Blot Analysis

Using a commercially available human-tissue dot-blot format, endogenous orphan GPCRs were probed for a determination of the areas where such receptors are localized. cDNA fragments from the GPCRs of Example 1 (radiolabelled) were (or can be) used as the probe: radiolabeled probe was (or can be) generated using the complete receptor cDNA (excised from the vector) using a Prime-It II™ Random Primer Labeling Kit (Stratagenc. 15 #300385), according to manufacturer's instructions. A human RNA Master Blot™ (Clontech. #7770-1) was hybridized with the endogenous human GPCR radiolabeled probe and washed under stringent conditions according manufacturer's instructions. The blot was exposed to Kodak BioMax™ Autoradiography film overnight at -80°C. Results are summarized for several receptors in Table B and C (see Figures 1A and 1B for a grid 20 identifying the various tissues and their locations, respectively). Exemplary dot-blots are provided in Figure 2A and 2B for results derived using hCHN3 and hCHN8, respectively.

TABLE B

##### ORPHAN GPCR

Tissue Distribution  
(highest levels, relative to other tissues in the dot-blot)

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|   |         |   |
|---|---------|---|
|   | hGPCR27 | Fetal brain, Putamen, Pituitary gland, Caudate nucleus          |
|   | hARE-1  | Spleen, Peripheral leukocytes, Fetal spleen                     |
|   | hPPR1   | Pituitary gland, Heart, salivary gland, Small intestine, Testis |
|   | hRUP3   | Pancreas  |
| 5 | hCHN3   | Fetal brain, Putamen, Occipital cortex                          |
|   | hCHN9   | Pancreas, Small intestine, Liver                                |
|   | hCHN10  | Kidney, Thryoid   |

TABLE C

| ORPHAN GPCR | Tissue Distribution<br>(highest levels, relative to other tissues in the dot-blot) |
|-------------|--|
| 10          | hARE-3 Cerebellum left, Cerebellum right, Testis, Accumbens                        |
|             | hGPCR3 Corpus collusum, Caudate nucleus, Liver, Heart, Inter-Ventricular Septum    |
|             | hARE-2 Cerebellum left, Cerebellum right, Substantia                               |
|             | hCHN8 Cerebellum left, Cerebellum right, Kidney, Lung                              |

## 2. RT-PCR

### 15 a. hRUP3

To ascertain the tissue distribution of hRUP3 mRNA, RT-PCR was performed using hRUP3-specific primers and human multiple tissue cDNA panels (MTC, Clontech) as templates. Taq DNA polymerase (Stratagene) was utilized for the PCR reaction, using the following reaction cycles in a 40ul reaction: 94°C for 2 min; 94°C for 15 sec; 55°C for 30 sec; 72°C for 1 min; 72°C, for 10 min. Primers were as follows:

5'-GACAGGTACCTTGCCATCAAG-3' (SEQ.ID.NO.: 61; sense)

5'-CTGCACAATGCCAGTGATAAGG-3' (SEQ.ID NO.: 62; antisense).

20ul of the reaction was loaded onto a 1% agarose gel; results are set forth in Figure 3.

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As is supported by the data of Figure 3, of the 16 human tissues in the cDNA panel utilized (brain, colon, heart, kidney, lung, ovary, pancreas, placenta, prostate, skeleton, small intestine, spleen, testis, thymus leukocyte, and liver) a single hRUP3 band is evident only from the pancreas. Additional comparative analysis of the protein sequence of hRUP3 with 5 other GPCRs suggest that hRUP3 is related to GPCRs having small molecule endogenous ligand such that it is predicted that the endogenous ligand for hRUP3 is a small molecule.

**b. hRUP4**

RT-PCR was performed using hRUP4 oligo's 8 and 4 as primers and the human multiple tissue cDNA panels (MTC, Clontech) as templates. Taq DNA polymerase 10 (Stratagene) was used for the amplification in a 40ul reaction by the following cycles: 94°C for 30 seconds, 94°C for 10 seconds, 55°C for 30 seconds, 72°C for 2 minutes, and 72°C for 5 minutes with cycles 2 through 4 repeated 30 times.

20  $\mu$ l of the reaction were loaded on a 1% agarose gel to analyze the RT-PCR products, and hRUP4 mRNA was found expressed in many human tissues, with the strongest 15 expression in heart and kidney. (see, Figure 4). To confirm the authenticity of the PCR fragments, a 300 bp fragment derived from the 5' end of hRUP4 was used as a probe for the Southern Blot analysis. The probe was labeled with  $^{32}$ P-dCTP using the Prime-It II<sup>TM</sup> Random Primer Labeling Kit (Stratagene) and purified using the ProbeQuant<sup>TM</sup> G-50 micro columns (Amersham). Hybridization was done overnight at 42° C following a 12 hr pre-20 hybridization. The blot was finally washed at 65°C with 0.1 x SSC. The Southern blot did confirm the PCR fragments as hRUP4.

**c. hRUP5**

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RT-PCR was performed using the following hRUP5 specific primers:

5'-CTGACTTCTTGTCCCTGGCAGCAGCGG-3' (SEQ.ID.NO.: 63; sense)

5'-AGACCAGCCAGGGCACGCTGAAGAGTG-3' (SEQ.ID.NO.: 64; antisense)

and the human multiple tissue cDNA panels (MTC, Clontech) as templates. Taq DNA polymerase (Stratagene) was used for the amplification in a 40ul reaction by the following cycles: 94°C for 30 sec, 94°C for 10 sec, 62°C for 1.5 min, 72°C for 5 min, and with cycles 2 through 3 repeated 30 times. 20 µl of the reaction were loaded on a 1.5% agarose gel to analyze the RT-PCR products, and hRUP5 mRNA was found expressed only in the peripheral blood leukocytes (*data not shown*).

10           d. hRUP6

RT-PCR was applied to confirm the expression and to determine the tissue distribution of hRUP6. Oligonucleotides used, based on an alignment of AC005871 and GPR66 segments, had the following sequences:

5'-CCAACACCAGCATCCATGGCATCAAG-3' (SEQ.ID.NO.: 73; sense),

15 5'-GGAGAGTCAGCTCTGAAAGAATTCAAGG-3' (SEQ.ID.NO.: 74; antisense)

and the human multiple tissue cDNA panels (MTC, Clontech) were used as templates.

PCR was performed using TaqPlus Precision™ polymerase (Stratagene; manufacturing instructions will be followed) in a 40ul reaction by the following cycles: 94°C for 30 sec; 94°C 5 sec; 66°C for 40 sec. 72°C for 2.5 min, and 72°C for 7 min. Cycles 2 through 4 were repeated 30 times.

20 ul of the reaction were loaded on a 1.2% agarose gel to analyze the RT-PCR products, and a specific 760bp DNA fragment representing hRUP6 was expressed predominantly in the thymus and with less expression in the heart, kidney, lung, prostate, small intestine and testis. (see, Figure 5).

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It is intended that each of the patents, applications, and printed publications mentioned in this patent document be hereby incorporated by reference in their entirety.

As those skilled in the art will appreciate, numerous changes and modifications may be made to the preferred embodiments of the invention without departing from the spirit of the invention. It is intended that all such variations fall within the scope of the invention and the claims that follow.

Although a variety of Vectors are available to those in the art, for purposes of utilization for both endogenous and non-endogenous human GPCRs, it is most preferred that the Vector utilized be pCMV. This vector was deposited with the American Type 10 Culture Collection (ATCC) on October 13, 1998 (10801 University Blvd., Manassas, VA 20110-2209 USA) under the provisions of the Budapest Treaty for the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure. The DNA was tested by the ATCC and determined to be. The ATCC has assigned the following deposit number to pCMV: ATCC #203351.

**CLAIMS**

What is claimed is:

1. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 1.
- 5 2. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 1 comprising SEQ.ID.NO.: 2.
3. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:1.
4. A Host Cell comprising the Plasmid of claim 3.
5. A cDNA encoding a human G protein-coupled receptor comprising 10 SEQ.ID.NO.: 3.
6. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 3 comprising SEQ.ID.NO.: 4.
7. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:3.
8. A Host Cell comprising the Plasmid of claim 7.
- 15 9. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 5.
10. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 5 comprising SEQ.ID.NO.: 6.
11. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:5.
- 20 12. A Host Cell comprising the Plasmid of claim 11
13. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 7.

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14. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 7 comprising SEQ.ID.NO.: 8.
15. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:7.
16. A Host Cell comprising the Plasmid of claim 15.
- 5 17. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 9.
18. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 9 comprising SEQ.ID.NO.: 10.
19. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:9.
- 10 20. A Host Cell comprising the Plasmid of claim 19.
21. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 11.
22. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 11 comprising SEQ.ID.NO.:12.
- 15 23. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:11.
24. A Host Cell comprising the Plasmid of claim 23.
25. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 13.
26. A human G protein-coupled receptor encoded by the cDNA of 20 SEQ.ID.NO.: 13 comprising SEQ.ID.NO.: 14.
27. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:13.
28. A Host Cell comprising the Plasmid of claim 27.
29. A cDNA encoding a human G protein-coupled receptor comprising

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SEQ.ID.NO.: 15.

30. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 15 comprising SEQ.ID.NO.: 16.

31. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:15.

5 32. A Host Cell comprising the Plasmid of claim 31.

33. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 17.

34. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 17 comprising SEQ.ID.NO.: 18.

10 35. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:17.

36. A Host Cell comprising the Plasmid of claim 35.

37. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 19.

38. A human G protein-coupled receptor encoded by the cDNA of 15 SEQ.ID.NO.: 19 comprising SEQ.ID.NO.: 20.

39. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:19.

40. A Host Cell comprising the Plasmid of claim 39.

41. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 21.

20 42. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 21 comprising SEQ.ID.NO.: 22.

43. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:21.

44. A Host Cell comprising the Plasmid of claim 43.

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45. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 23.

46. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 23 comprising SEQ.ID.NO.: 24.

5 47. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.: 23.

48. A Host Cell comprising the Plasmid of claim 47.

49. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 25.

50. A human G protein-coupled receptor encoded by the cDNA of  
10 SEQ.ID.NO.: 25 comprising SEQ.ID.NO.: 26.

51. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:25.

52. A Host Cell comprising the Plasmid of claim 51.

53. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 27.

15 54. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 27 comprising SEQ.ID.NO.: 28.

55. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:27.

56. A Host Cell comprising the Plasmid of claim 55.

57. A cDNA encoding a human G protein-coupled receptor comprising  
20 SEQ.ID.NO.: 29.

58. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 29 comprising SEQ.ID.NO.: 30.

59. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:29.

- 35 -

60. A Host Cell comprising the Plasmid of claim 59.
61. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 31.
62. A human G protein-coupled receptor encoded by the cDNA of 5 SEQ.ID.NO.: 31 comprising SEQ.ID.NO.: 32.
63. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:31.
64. A Host Cell comprising the Plasmid of claim 63.
65. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 33.

10        66. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 33 comprising SEQ.ID.NO.: 34.

67. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:33.
68. A Host Cell comprising the Plasmid of claim 67.
69. A cDNA encoding a human G protein-coupled receptor comprising 15 SEQ.ID.NO.: 35.

70. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 35 comprising SEQ.ID.NO.: 36.

71. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:35.
72. A Host Cell comprising the Plasmid of claim 71.

20        73. A cDNA encoding a human G protein-coupled receptor comprising SEQ.ID.NO.: 37.

74. A human G protein-coupled receptor encoded by the cDNA of SEQ.ID.NO.: 37 comprising SEQ.ID.NO.: 38.

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75. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:37.
76. A Host Cell comprising the Plasmid of claim 75.

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|   | 1                | 2               | 3                | 4               | 5              | 6                    | 7                 | 8             |
|---|------------------|-----------------|------------------|-----------------|----------------|----------------------|-------------------|---------------|
| A | Amygdala         | Caudate Nucleus | Cerebellum       | Cerebral Cortex | Frontal Cortex | Hippocampus          | Medulla Oblongata |               |
| B | Occipital Cortex | Putamen         | Substantia Nigra | Temporal Cortex | Thalamus       | Accumbens            | Spinal Cord       |               |
| C | Heart            | Aorta           | Skeletal Muscle  | Colon           | Bladder        | Uterus               | Prostate          | Stomach       |
| D | Testis           | Ovary           | Pancreas         | Pituitary       | Adrenal Gland  | Thyroid              | Salivary Gland    | Mammary Gland |
| E | Kidney           | Liver           | Small Intestine  | Spleen          | Thymus         | Peripheral Leukocyte | Lymph Node        | Bone Marrow   |
| F | Appendix         | Lung            | Trachea          | Placenta        |                |                      |                   |               |
| G | Fetal Brain      | Fetal Heart     | Fetal Kidney     | Fetal Liver     | Fetal Spleen   | Fetal Thymus         | Fetal Lung        |               |
| H |                  |                 |                  |                 |                |                      |                   |               |

FIG. 1A

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|   | 1   | 2                    | 3                  | 4                              | 5                   | 6      | 7                       | 8        | 9                 | 10                                    | 11              | 12 |
|---|---|----------------------|--------------------|--------------------------------|---------------------|--------|-------------------------|----------|-------------------|---------------------------------------|-----------------|----|
| A | Cerebellum<br>Left                            | Substantia<br>Nigra  | Heart              | Esophagus                      | Colon<br>Transverse | Kidney | Lung                    | Liver    | Leukemia<br>HL-60 | Fetal<br>Brain                        |                 |    |
| B | Cerebral<br>Cortex                            | Cerebellum<br>Right  | Accumbens          | Aorta                          | Stomach             | Colon  | Skeletal<br>Muscle      | Pancreas | HeLa S3           | Fetal<br>Heart                        |                 |    |
| C | Frontal<br>Cortex                             | Corpus<br>Callosum   | Thalamus           | Atrium<br>Left                 | Duodenum            | Rectum | Spleen                  | Bladder  | Adrenal<br>Gland  | Leukemia<br>K562                      | Fetal<br>Kidney |    |
| D | Parietal<br>Lobe                              | Amygdala             | Pituitary<br>Gland | Atrium<br>Right                | Jejunum             |        | Thymus                  | Uterus   | Thyroid           | Leukemia<br>MOLT-4                    | Fetal<br>Liver  |    |
| E | Occipital<br>Cortex                           | Claudete             | Spinal<br>Cord     | Ventricle<br>Left              | Ileum               |        | Peripheral<br>Leukocyte | Prostate | Salivary<br>Gland | Burkitt's<br>Lymphoma<br>Raji         | Fetal<br>Spleen |    |
| F | Temporal<br>Cortex                            | Hippocampus          |                    | Ventricle<br>Right             | Ileocecum           |        | Lymph<br>Node           | Testis   | Mammary<br>Gland  | Burkitt's<br>Lymphoma<br>Daudi        | Fetal<br>Thymus |    |
| G | Paracentral<br>Gyrus of<br>Cerebral<br>Cortex | Medulla<br>Oblongata |                    | Inter<br>Ventricular<br>Septum | Appendix            |        | Bone<br>Marrow          | Ovary    |                   | Colorectal<br>Adenocarcinoma<br>SW480 | Fetal<br>Lung   |    |
| H | Pons  | Putamen              |                    | Apex of<br>the Heart           | Colon<br>Ascending  |        | Trachea                 |          |                   | Lung<br>Carcinoma<br>A549             |                 |    |

SUBSTITUTE SHEET (RULE 26)

FIG. 1B

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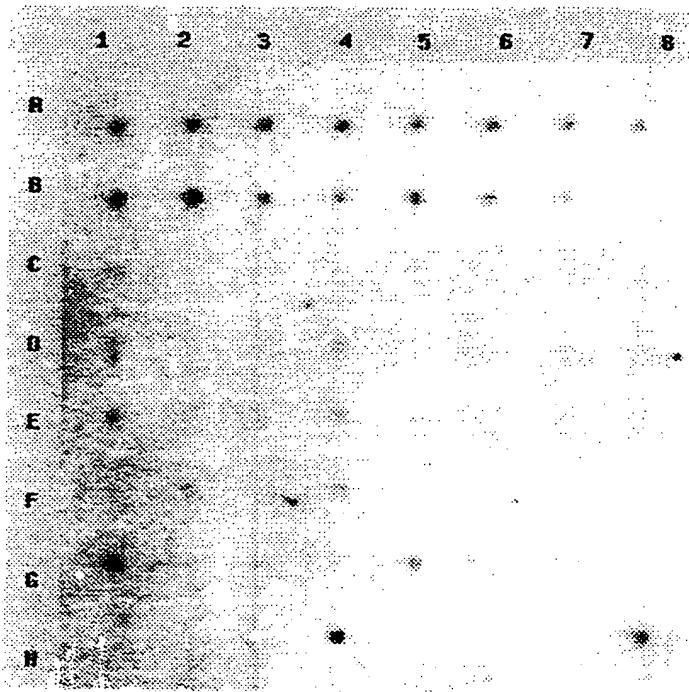


FIG. 2A

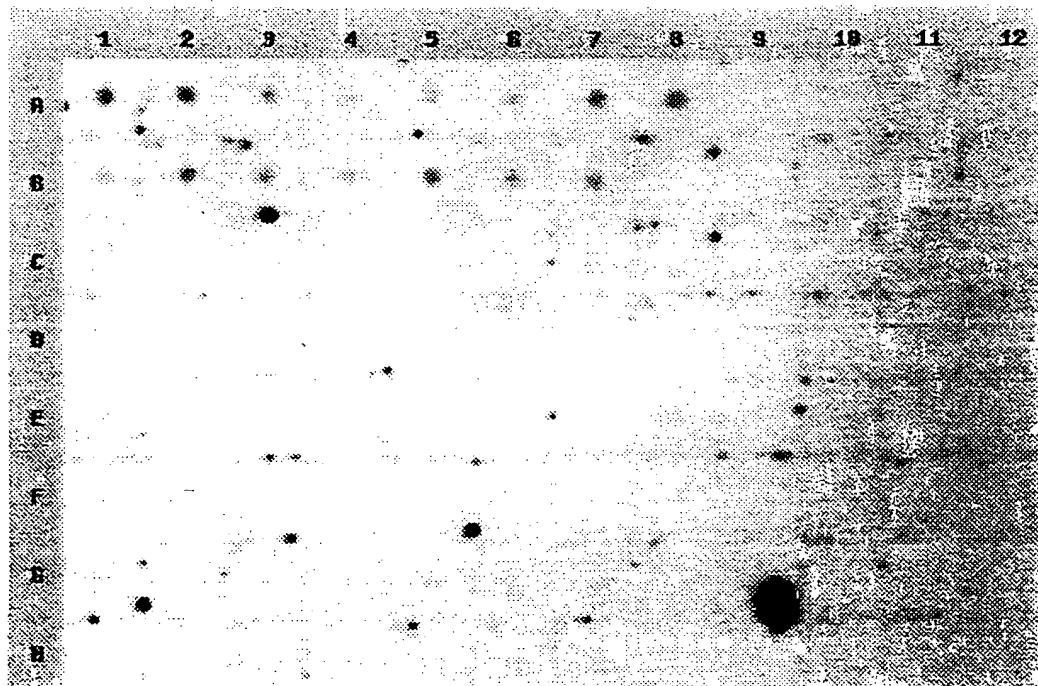
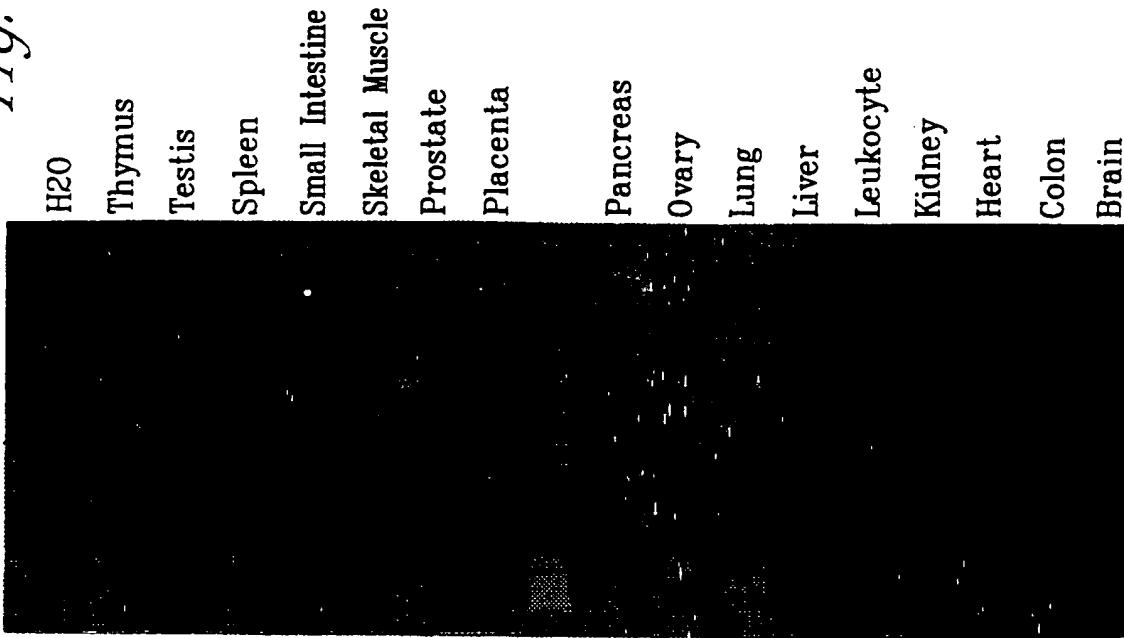


FIG. 2B

SUBSTITUTE SHEET (RULE 26)

FIG. 5



*FIG. 3*   
*FIG. 4*

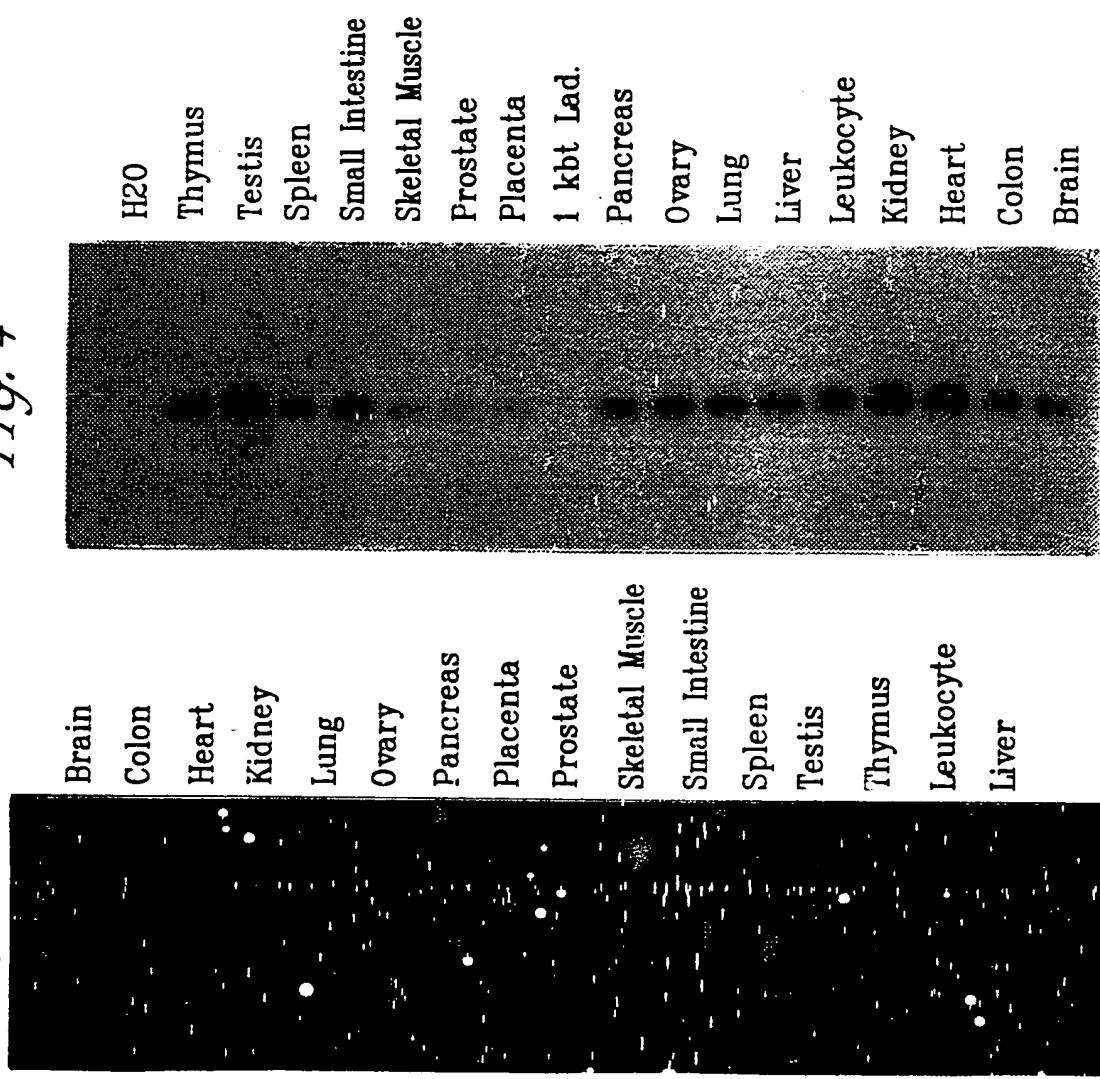
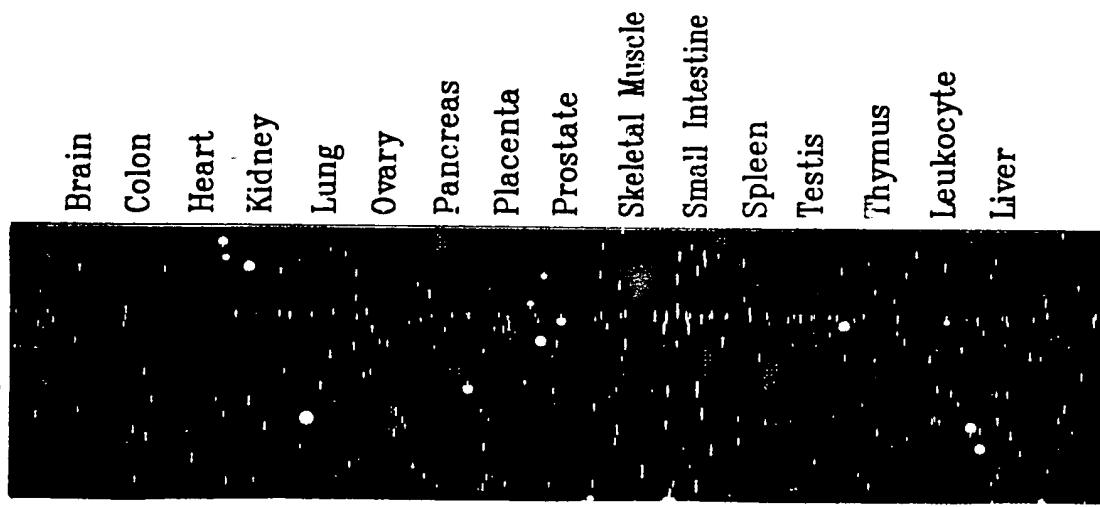


FIG. 3



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## SEQUENCE LISTING

## (1) GENERAL INFORMATION:

(i) APPLICANT: Chen, Ruoping  
Dang, Huong T.  
5 Liaw, Chen W.  
Lin, I-Lin

(ii) TITLE OF INVENTION: Human Orphan G Protein-Coupled Receptors

(iii) NUMBER OF SEQUENCES: 74

## 10 (iv) CORRESPONDENCE ADDRESS:

(A) ADDRESSEE: Arena Pharmaceuticals, Inc.  
(B) STREET: 6166 Nancy Ridge Drive  
(C) CITY: San Diego  
(D) STATE: CA  
15 (E) COUNTRY: USA  
(F) ZIP: 92121

## (v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk  
(B) COMPUTER: IBM PC compatible  
20 (C) OPERATING SYSTEM: PC-DOS/MS-DOS  
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30

## (vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: US  
(B) FILING DATE:  
25 (C) CLASSIFICATION:

## (vii) ATTORNEY/AGENT INFORMATION:

(A) NAME: Burgoon, Richard P.  
(B) REGISTRATION NUMBER: 34,787

## (ix) TELECOMMUNICATION INFORMATION:

30 (A) TELEPHONE: (858)453-7200  
(B) TELEFAX: (858)453-7210

## (2) INFORMATION FOR SEQ ID NO:1:

## (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1260 base pairs  
35 (B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

40 ATGGTCTTCT CGGCAGTGTT GACTGCGTTC CATACCGCTGA CATCCAACAC AACATTTGTC 60

- 2 -

GTGTATGAAA ACACCTACAT GAATATTACA CTCCCTCCAC CATTCCAGCA TCCTGACCTC 120  
 AGTCCATTGC TTAGATATAG TTTGAAACC ATGGCTCCA CTGGTTGAG TTCCTTGACC 180  
 GTGAATAGTA CAGCTGTGCC CACAAACACCA GCAGCATTAA AGAGCCTAAA CTTGCCTCTT 240  
 CAGATCACCC TTTCTGCTAT AATGATATTTC ATTCTGTTG TGTCTTTCT TGGGAACCTG 300  
 5 GTTGTGTTGCC TCATGGTTA CCAAAAAGCT GCCATGAGGT CTGCAATTAA CATCCTCCTT 360  
 GCCAGCCTAG CTTTGAGA CATGTTGCTT GCAGTGCTGA ACATGCCCTT TGCCCTGGTA 420  
 ACTATTCTTA CTACCCGATG GATTTTGGG AAATTCTTCT GTAGGGTATC TGCTATGTTT 480  
 TTCTGGTTAT TTGTGATAGA AGGAGTAGCC ATCCTGCTCA TCATTAGCAT AGATAGGTT 540  
 CTTATTATAG TCCAGAGGCA GGATAAGCTA AACCCATATA GAGCTAAGGT TCTGATTGCA 600  
 10 GTTTCTTGGG CAACTTCCTT TTGTGTAGCT TTTCTTTAG CGTAGGAAA CCCCGACCTG 660  
 CAGATAACCTT CCCGAGCTCC CCAGTGTGTG TTTGGGTACA CAACCAATCC AGGCTACCAG 720  
 GCTTATGTGA TTTTGATTTC TCTCATTCT TTCTTCATAC CCTTCCTGGT AATACTGTAC 780  
 TCATTTATGG GCATACTCAA CACCCCTCGG CACAATGCCT TGAGGATCCA TAGCTACCC 840  
 GAAGGTATAT GCCTCAGCCA GGCCAGCAA CTGGGTCTCA TGAGTCTGCA GAGACCTTTC 900  
 15 CAGATGAGCA TTGACATGGG CTTTAAAACA CGTGCCTTCA CCACTATTTT GATTCTCTT 960  
 GCTGTCTTCA TTGTCTGCTG GGCCCCATTC ACCACTTACA GCCTTGTGGC  
 AACATTCAAGT1020  
 AAGCACTTTT ACTATCAGCA CAACTTTTT GAGATTAGCA CCTGGCTACT GTGGCTCTGC1080  
 TACCTCAAGT CTGCATTGAA TCCGCTGATC TACTACTGGA GGATTAAGAA ATTCCATGAT1140  
 20 GCTTGCCTGG ACATGATGCC TAAGTCCTTC AAGTTTTGC CGCAGCTCCC TGGTCACACA1200  
 AAGCGACGGA TACGTCTAG TGCTGTCTAT GTGTGTGGGG AACATCGGAC GGTGGTGTGA1260

(3) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 419 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic).

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

30 Met Val Phe Ser Ala Val Leu Thr Ala Phe His Thr Gly Thr Ser Asn  
                   1               5               10               15

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|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Thr | Thr | Phe | Val | Val | Tyr | Glu | Asn | Thr | Tyr | Met | Asn | Ile | Thr | Leu | Pro |
|    |     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
|    | Pro | Pro | Phe | Gln | His | Pro | Asp | Leu | Ser | Pro | Leu | Leu | Arg | Tyr | Ser | Phe |
|    |     |     |     | 35  |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| 5  | Glu | Thr | Met | Ala | Pro | Thr | Gly | Leu | Ser | Ser | Leu | Thr | Val | Asn | Ser | Thr |
|    |     |     |     | 50  |     |     |     | 55  |     |     |     | 60  |     |     |     |     |
|    | Ala | Val | Pro | Thr | Thr | Pro | Ala | Ala | Phe | Lys | Ser | Leu | Asn | Leu | Pro | Leu |
|    |     |     |     | 65  |     |     |     | 70  |     |     |     | 75  |     |     | 80  |     |
| 10 | Gln | Ile | Thr | Leu | Ser | Ala | Ile | Met | Ile | Phe | Ile | Leu | Phe | Val | Ser | Phe |
|    |     |     |     | 85  |     |     |     | 90  |     |     |     | 95  |     |     |     |     |
|    | Leu | Gly | Asn | Leu | Val | Val | Cys | Leu | Met | Val | Tyr | Gln | Lys | Ala | Ala | Met |
|    |     |     |     | 100 |     |     |     | 105 |     |     |     | 110 |     |     |     |     |
|    | Arg | Ser | Ala | Ile | Asn | Ile | Leu | Leu | Ala | Ser | Leu | Ala | Phe | Ala | Asp | Met |
|    |     |     |     | 115 |     |     |     | 120 |     |     |     | 125 |     |     |     |     |
| 15 | Leu | Leu | Ala | Val | Leu | Asn | Met | Pro | Phe | Ala | Leu | Val | Thr | Ile | Leu | Thr |
|    |     |     |     | 130 |     |     |     | 135 |     |     |     | 140 |     |     |     |     |
|    | Thr | Arg | Trp | Ile | Phe | Gly | Lys | Phe | Phe | Cys | Arg | Val | Ser | Ala | Met | Phe |
|    |     |     |     | 145 |     |     |     | 150 |     |     |     | 155 |     |     | 160 |     |
| 20 | Phe | Trp | Leu | Phe | Val | Ile | Glu | Gly | Val | Ala | Ile | Leu | Leu | Ile | Ile | Ser |
|    |     |     |     | 165 |     |     |     | 170 |     |     |     | 175 |     |     |     |     |
|    | Ile | Asp | Arg | Phe | Leu | Ile | Ile | Val | Gln | Arg | Gln | Asp | Lys | Leu | Asn | Pro |
|    |     |     |     | 180 |     |     |     | 185 |     |     |     | 190 |     |     |     |     |
|    | Tyr | Arg | Ala | Lys | Val | Leu | Ile | Ala | Val | Ser | Trp | Ala | Thr | Ser | Phe | Cys |
|    |     |     |     | 195 |     |     |     | 200 |     |     |     | 205 |     |     |     |     |
| 25 | Val | Ala | Phe | Pro | Leu | Ala | Val | Gly | Asn | Pro | Asp | Leu | Gln | Ile | Pro | Ser |
|    |     |     |     | 210 |     |     |     | 215 |     |     |     | 220 |     |     |     |     |
|    | Arg | Ala | Pro | Gln | Cys | Val | Phe | Gly | Tyr | Thr | Asn | Pro | Gly | Tyr | Gln |     |
|    |     |     |     | 225 |     |     |     | 230 |     |     |     | 235 |     |     | 240 |     |
| 30 | Ala | Tyr | Val | Ile | Leu | Ile | Ser | Leu | Ile | Ser | Phe | Phe | Ile | Pro | Phe | Leu |
|    |     |     |     | 245 |     |     |     | 250 |     |     |     | 255 |     |     |     |     |
|    | Val | Ile | Leu | Tyr | Ser | Phe | Met | Gly | Ile | Leu | Asn | Thr | Leu | Arg | His | Asn |
|    |     |     |     | 260 |     |     |     | 265 |     |     |     | 270 |     |     |     |     |
|    | Ala | Leu | Arg | Ile | His | Ser | Tyr | Pro | Glu | Gly | Ile | Cys | Leu | Ser | Gln | Ala |
|    |     |     |     | 275 |     |     |     | 280 |     |     |     | 285 |     |     |     |     |
| 35 | Ser | Lys | Leu | Gly | Leu | Met | Ser | Leu | Gln | Arg | Pro | Phe | Gln | Met | Ser | Ile |
|    |     |     |     | 290 |     |     |     | 295 |     |     |     | 300 |     |     |     |     |
|    | Asp | Met | Gly | Phe | Lys | Thr | Arg | Ala | Phe | Thr | Ile | Leu | Ile | Leu | Phe |     |

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|    |   |     |     |     |
|----|---|-----|-----|-----|
|    | 305   | 310 | 315 | 320 |
|    | Ala Val Phe Ile Val Cys Trp Ala Pro Phe Thr Thr Tyr Ser Leu Val |     |     |     |
|    | 325   | 330 | 335 |     |
| 5  | Ala Thr Phe Ser Lys His Phe Tyr Tyr Gln His Asn Phe Phe Glu Ile |     |     |     |
|    | 340   | 345 | 350 |     |
|    | Ser Thr Trp Leu Leu Trp Leu Cys Tyr Leu Lys Ser Ala Leu Asn Pro |     |     |     |
|    | 355   | 360 | 365 |     |
|    | Leu Ile Tyr Tyr Trp Arg Ile Lys Lys Phe His Asp Ala Cys Leu Asp |     |     |     |
|    | 370   | 375 | 380 |     |
| 10 | Met Met Pro Lys Ser Phe Lys Phe Leu Pro Gln Leu Pro Gly His Thr |     |     |     |
|    | 385   | 390 | 395 | 400 |
|    | Lys Arg Arg Ile Arg Pro Ser Ala Val Tyr Val Cys Gly Glu His Arg |     |     |     |
|    | 405   | 410 | 415 |     |
|    | Thr Val Val   |     |     |     |
| 15 |   |     |     |     |

## (4) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1119 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
  
- (ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

```

ATGTTAGCCA ACAGCTCCTC AACCAACAGT TCTGTTCTCC CGTGTCTGA CTACCGACCT 60
25 ACCCACCGCC TGCACTTGGT GGTCTACAGC TTGGTGCTGG CTGCCGGGCT CCCCCCTCAAC 120
GCGCTAGCCC TCTGGGTCTT CCTGCGCGCG CTGCGCGTGC ACTCGGTGGT GAGCGTGTAC 180
ATGTGTAACC TGGCGGCCAG CGACCTGCTC TTCACCCCTCT CGCTGCCGT TCGTCTCTCC 240
TACTACGCAC TGCACCACTG GCCCTTCCCC GACCTCCTGT GCCAGACGAC GGGCGCCATC 300
TTCCAGATGA ACATGTACGG CAGCTGCATC TTCTGATGC TCATCAACGT GGACCGCTAC 360
30 GCCGCCATCG TGCACCCGCT GCGACTGCGC CACCTGCGGC GGCCCCGGT GGCGCGGCTG 420
CTCTGCCCTGG GCGTGTGGGC GCTCATCCTG GTGTTTGCCG TGCCCGCCGC CCGCGTGCAC 480
AGGCCCTCGC GTTGCCGCTA CCGGGACCTC GAGGTGCGCC TATGCTTCGA GAGCTTCAGC 540
GACGAGCTGT GGAAAGGCAG GCTGCTGCC CTCGTGCTGC TGGCCGAGGC GCTGGGCTTC 600

```

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CTGCTGCCCT TGGCGCGGGT GGTCTACTCG TCGGGCCGAG TCTTCGGAC GCTGGCGCGC 660  
 CCCGACGCCA CGCAGAGCCA GCGCGGGCGG AAGACCGTGC GCCTCCTGCT GGCTAACCTC 720  
 GTCATCTTCC TGCTGTGCTT CGTGCCCTAC AACAGCACGC TGGCGGTCTA CGGGCTGCTG 780  
 CGGAGCAAGC TGGTGGCGC CAGCGTGCCT GCCCCGCGATC GCGTGCACGG GGTGCTGATG 840  
 5 GTGATGGTGC TGCTGGCCGG CGCCAACCTGC GTGCTGGACC CGCTGGTGTAA CTACTTTAGC 900  
 GCCGAGGGCT TCCGCAACAC CCTGCGCGGC CTGGGCACTC CGCACCGGGC CAGGACCTCG 960  
 GCCACCAACG GGACCGGGC GGCGCTCGCG CAATCCGAAA GGTCCGCCGT CACCACCGAC 1020  
 GCCACCAAGC CGGATGCCGC CAGTCAGGGG CTGCTCCGAC CCTCCGACTC CCACCTCTG 1080  
 TCTTCCTTCA CACAGTGTCC CCAGGATTCC GCCCTCTGA 1119

10 (5) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 372 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:  
 15 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Met | Leu | Ala | Asn | Ser | Ser | Ser | Thr | Asn | Ser | Ser | Val | Leu | Pro | Cys | Pro |
|    | 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     | 15  |     |     |
| 20 | Asp | Tyr | Arg | Pro | Thr | His | Arg | Leu | His | Leu | Val | Val | Tyr | Ser | Leu | Val |
|    |     |     |     |     | 20  |     |     |     |     | 25  |     |     |     | 30  |     |     |
|    | Leu | Ala | Ala | Gly | Leu | Pro | Leu | Asn | Ala | Leu | Ala | Leu | Trp | Val | Phe | Leu |
|    |     |     |     |     | 35  |     |     |     |     | 40  |     |     |     | 45  |     |     |
| 25 | Arg | Ala | Leu | Arg | Val | His | Ser | Val | Val | Ser | Val | Tyr | Met | Cys | Asn | Leu |
|    |     |     |     |     | 50  |     |     |     |     | 55  |     |     |     | 60  |     |     |
|    | Ala | Ala | Ser | Asp | Leu | Leu | Phe | Thr | Leu | Ser | Leu | Pro | Val | Arg | Leu | Ser |
|    |     |     |     |     | 65  |     |     |     |     | 70  |     |     |     | 75  |     | 80  |
|    | Tyr | Tyr | Ala | Leu | His | His | Trp | Pro | Phe | Pro | Asp | Leu | Leu | Cys | Gln | Thr |
|    |     |     |     |     | 85  |     |     |     |     | 90  |     |     |     | 95  |     |     |
| 30 | Thr | Gly | Ala | Ile | Phe | Gln | Met | Asn | Met | Tyr | Gly | Ser | Cys | Ile | Phe | Leu |
|    |     |     |     |     | 100 |     |     |     |     | 105 |     |     |     | 110 |     |     |
|    | Met | Leu | Ile | Asn | Val | Asp | Arg | Tyr | Ala | Ala | Ile | Val | His | Pro | Leu | Arg |
|    |     |     |     |     | 115 |     |     |     |     | 120 |     |     |     | 125 |     |     |

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|    |   |     |     |     |
|----|---|-----|-----|-----|
|    | Leu Arg His Leu Arg Arg Pro Arg Val Ala Arg Leu Leu Cys Leu Gly |     |     |     |
|    | 130   | 135 | 140 |     |
|    | Val Trp Ala Leu Ile Leu Val Phe Ala Val Pro Ala Ala Arg Val His |     |     |     |
|    | 145   | 150 | 155 | 160 |
| 5  | Arg Pro Ser Arg Cys Arg Tyr Arg Asp Ieu Glu Val Arg Leu Cys Phe |     |     |     |
|    | 165   | 170 | 175 |     |
|    | Glu Ser Phe Ser Asp Glu Leu Trp Lys Gly Arg Leu Leu Pro Leu Val |     |     |     |
|    | 180   | 185 | 190 |     |
| 10 | Leu Leu Ala Glu Ala Leu Gly Phe Leu Leu Pro Leu Ala Ala Val Val |     |     |     |
|    | 195   | 200 | 205 |     |
|    | Tyr Ser Ser Gly Arg Val Phe Trp Thr Leu Ala Arg Pro Asp Ala Thr |     |     |     |
|    | 210   | 215 | 220 |     |
|    | Gln Ser Gln Arg Arg Arg Lys Thr Val Arg Leu Leu Leu Ala Asn Leu |     |     |     |
|    | 225   | 230 | 235 | 240 |
| 15 | Val Ile Phe Leu Leu Cys Phe Val Pro Tyr Asn Ser Thr Leu Ala Val |     |     |     |
|    | 245   | 250 | 255 |     |
|    | Tyr Gly Leu Leu Arg Ser Lys Leu Val Ala Ala Ser Val Pro Ala Arg |     |     |     |
|    | 260   | 265 | 270 |     |
| 20 | Asp Arg Val Arg Gly Val Leu Met Val Met Val Leu Leu Ala Gly Ala |     |     |     |
|    | 275   | 280 | 285 |     |
|    | Asn Cys Val Leu Asp Pro Leu Val Tyr Tyr Phe Ser Ala Glu Gly Phe |     |     |     |
|    | 290   | 295 | 300 |     |
|    | Arg Asn Thr Leu Arg Gly Leu Gly Thr Pro His Arg Ala Arg Thr Ser |     |     |     |
|    | 305   | 310 | 315 | 320 |
| 25 | Ala Thr Asn Gly Thr Arg Ala Ala Leu Ala Gln Ser Glu Arg Ser Ala |     |     |     |
|    | 325   | 330 | 335 |     |
|    | Val Thr Thr Asp Ala Thr Arg Pro Asp Ala Ala Ser Gln Gly Leu Leu |     |     |     |
|    | 340   | 345 | 350 |     |
| 30 | Arg Pro Ser Asp Ser His Ser Leu Ser Ser Phe Thr Gln Cys Pro Gln |     |     |     |
|    | 355   | 360 | 365 |     |
|    | Asp Ser Ala Leu   |     |     |     |
|    | 370   |     |     |     |

## (6) INFORMATION FOR SEQ ID NO:5:

35 (1) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1107 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

ATGGCCAACCT CCACAGGGCT GAACGCCTCA GAAGTCGCAG GCTCGTTGGG GTTGATCCTG 60  
GCAGCTGTCG TGGAGGTGGG GGCACTGCTG GGCAACGGCG CGCTGCTGGT CGTGGTGCTG 120  
5 CGCACGCCGG GACTGCGCGA CGCGCTCTAC CTGGCGCACC TGTGCGTCGT GGACCTGCTG 180  
CGGGCCGCCT CCATCATGCC GCTGGGCCTG CTGGCCGCAC CGCCGCCCGG GCTGGGCCGC 240  
GTGCGCCTGG GCCCGCGGCC ATGCCCGGCC GCTCGCTTCC TCTCCGCCGC TCTGCTGCCG 300  
GCCTGCACGC TCAGGGGTGGC CGCAGTTGGC CTGGCACGCT ACCGCCTCAT CGTGCACCCG 360  
CTGCGGCCAG GCTCGCGGCC GCCGCCTGTG CTCGTGCTCA CGGCCGTGTG GGCCGCCGGCG 420  
10 GGACTGCTGG GCGCGCTCTC CCTGCTCGGC CGGCCGCCCG CACCGCCCCC TGCTCCTGCT 480  
CGCTGCTCGG TCCTGGCTGG GGGCCTCGGG CCCTTCCGGC CGCTCTGGC CCTGCTGGCC 540  
TTCGCGCTGC CGGCCCTCCT GCTGCTCGGC GCCTACGGCG GCATCTTCGT GGTGGCGCGT 600  
CGCGCTGCCCG TGAGGGCCCC ACGGCCGGCG CGCGGGTCCC GACTCCGCTC GGACTCTCTG 660  
GATAGCCGCC TTTCCATCTT GCCGCCGCTC CGGCCTCGCC TGCCCCGGGG CAAGGCGGCC 720  
15 CTGGCCCCAG CGCTGGCCGT GGGCAAATTG GCAGCCTGCT GGCTGCCCTA TGGCTGCGCG 780  
TGCCCTGGCGC CGCGAGCGCG GGCGCGGAA GCCGAAGCGG CTGTCACCTG GGTCGCCTAC 840  
TCGGCCCTCG CGGCTCACCC CTTCCGTAC GGGCTGCTGC AGCGCCCCGT GCGCTTGGCA 900  
CTGGGCCGCC TCTCTCGCCG TGCACTGCCT GGACCTGTGC GGGCCTGCAC TCCGCAAGCC 960  
TGGCACCCGC GGGCACTCTT GCAATGCCTC CAGAGACCCC CAGAGGGCCC TGCCGTAGGC 1020  
20 CCTTCTGAGG CTCCAGAACAA GACCCCCGAG TTGGCAGGAG GGCGGAGCCC CGCATACCAG 1080  
GGGCCACCTG AGAGTTCTCT CTCCTGA 1107

(7) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 368 amino acids  
(B) TYPE: amino acid  
(C) STRANDEDNESS:  
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

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|    |   |     |
|----|---|-----|
|    | Met Ala Asn Ser Thr Gly Leu Asn Ala Ser Glu Val Ala Gly Ser Leu |     |
| 1  | 5   | 10  |
|    | 15  |     |
|    | Gly Leu Ile Leu Ala Ala Val Val Glu Val Gly Ala Leu Leu Gly Asn |     |
|    | 20  | 25  |
|    | 30  |     |
| 5  | Gly Ala Leu Leu Val Val Val Leu Arg Thr Pro Gly Leu Arg Asp Ala |     |
|    | 35  | 40  |
|    | 45  |     |
|    | Leu Tyr Leu Ala His Leu Cys Val Val Asp Leu Leu Ala Ala Ala Ser |     |
|    | 50  | 55  |
|    | 60  |     |
| 10 | Ile Met Pro Leu Gly Leu Leu Ala Ala Pro Pro Pro Gly Leu Gly Arg |     |
|    | 65  | 70  |
|    | 75  | 80  |
|    | Val Arg Leu Gly Pro Ala Pro Cys Arg Ala Ala Arg Phe Leu Ser Ala |     |
|    | 85  | 90  |
|    | 95  |     |
|    | Ala Leu Leu Pro Ala Cys Thr Leu Gly Val Ala Ala Leu Gly Leu Ala |     |
|    | 100   | 105 |
|    | 110   |     |
| 15 | Arg Tyr Arg Leu Ile Val His Pro Leu Arg Pro Gly Ser Arg Pro Pro |     |
|    | 115   | 120 |
|    | 125   |     |
|    | Pro Val Leu Val Leu Thr Ala Val Trp Ala Ala Ala Gly Leu Leu Gly |     |
|    | 130   | 135 |
|    | 140   |     |
| 20 | Ala Leu Ser Leu Leu Gly Pro Pro Pro Ala Pro Pro Pro Ala Pro Ala |     |
|    | 145   | 150 |
|    | 155   | 160 |
|    | Arg Cys Ser Val Leu Ala Gly Gly Leu Gly Pro Phe Arg Pro Leu Trp |     |
|    | 165   | 170 |
|    | 175   |     |
|    | Ala Leu Leu Ala Phe Ala Leu Pro Ala Leu Leu Leu Gly Ala Tyr     |     |
|    | 180   | 185 |
|    | 190   |     |
| 25 | Gly Gly Ile Phe Val Val Ala Arg Arg Ala Ala Leu Arg Pro Pro Arg |     |
|    | 195   | 200 |
|    | 205   |     |
|    | Pro Ala Arg Gly Ser Arg Leu Arg Ser Asp Ser Leu Asp Ser Arg Leu |     |
|    | 210   | 215 |
|    | 220   |     |
| 30 | Ser Ile Leu Pro Pro Leu Arg Pro Arg Leu Pro Gly Gly Lys Ala Ala |     |
|    | 225   | 230 |
|    | 235   | 240 |
|    | Leu Ala Pro Ala Leu Ala Val Gly Gln Phe Ala Ala Cys Trp Leu Pro |     |
|    | 245   | 250 |
|    | 255   |     |
|    | Tyr Gly Cys Ala Cys Leu Ala Prc Ala Ala Arg Ala Ala Glu Ala Glu |     |
|    | 260   | 265 |
|    | 270   |     |
| 35 | Ala Ala Val Thr Trp Val Ala Tyr Ser Ala Phe Ala Ala His Pro Phe |     |
|    | 275   | 280 |
|    | 285   |     |
|    | Leu Tyr Gly Leu Leu Gln Arg Pro Val Arg Leu Ala Leu Gly Arg Leu |     |

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290

295

300

Ser Arg Arg Ala Leu Pro Gly Pro Val Arg Ala Cys Thr Pro Gln Ala  
305 310 315 320

Trp His Pro Arg Ala Leu Leu Gln Cys Leu Gln Arg Pro Pro Glu Gly  
325 330 335

Pro Ala Val Gly Pro Ser Glu Ala Pro Glu Gln Thr Pro Glu Leu Ala  
340 345 350

Gly Gly Arg Ser Pro Ala Tyr Gln Gly Prc Pro Glu Ser Ser Leu Ser  
355 360 365

10 (8) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 1008 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- ii) MOLECULE TYPE: DNA (genomic)

### (vi) SEQUENCE DESCRIPTION: SEQ ID NO: 11

ATGGAATCAT CTTTCTCATT TGGAGTGATC CTTGCTGTCC TGGCCTCCCT CATCATTGCT 60  
ACTAACACAC TAGTGGCTGT GGCTGTGCTG CTGTTGATCC ACAAGAATGA TGGTGTCACT 120  
20 CTCTGCTTCA CCTTGAATCT GGCTGTGGCT GACACCTTGA TTGGTGTGGC CATCTCTGGC 180  
CTACTCACAG ACCAGCTCTC CAGCCCTTCT CGGCCACAC AGAAGACCC GTGCAGCCTG 240  
CGGATGGCAT TTGTCACTTC CTCCGCAGCT GCCTCTGTCC TCACGGTCAT GCTGATCACC 300  
TTTGACAGGT ACCTTGCCAT CAAGCAGCCC TTCCGCTACT TGAAGATCAT GAGTGGGTTTC 360  
GTGGCCGGGG CCTGCATTGC CGGGCTGTGG TTAGTGTCTT ACCTCATTGG CTTCCTCCCA 420  
25 CTCGGAATCC CCATGTTCCA GCAGACTGCC TACAAAGGGC AGTGCAGCTT CTTTGCTGTA 480  
TTTCACCCCTC ACTTCGTGCT GACCCTCTCC TGCCTGGCT TCTTCCCAGC CATGCTCCTC 540  
TTTGTCTTCT TCTACTGCGA CATGCTCAAG ATTGCCTCCA TGACACGCCA GCAGATTCGA 600  
AAGATGGAAC ATGCAGGAGC CATGGCTGGA GGTTATCGAT CCCCACGGAC TCCCAGCGAC 660  
TTCAAAGCTC TCCGTACTGT GTCTGTTCTC ATTGGGAGCT TTGCTCTATC CTGGACCCCC 720  
30 TTCCTTATCA CTGGCATTGT GCAGGGTGGCC TGCCAGGAGT GTCACCTCTA CCTAGTGTGCT 780  
GAACGGTACC TGTGGCTGCT CGGCGTGGGC AACTCCCTGC TCAACCCACT CATCTATGCC 840

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TATTGGCAGA AGGAGGTGCG ACTGCAGCTC TACCACATGG CCCTAGGAGT GAAGAAGGTG 900  
CTCACCTCAT TCCTCCTCTT TCTCTCGGCC AGGAATTGTG GCCCAGAGAG GCCCAGGGAA 960  
AGTTCCCTGTC ACATCGTCAC TATCTCCAGC TCAGAGTTTG ATGGCTAA 1008

(9) INFORMATION FOR SEQ ID NO:8:

5 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 335 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: not relevant

10 (ii) MOLECULE TYPE: protein

10 (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Glu Ser Ser Phe Ser Phe Gly Val Ile Leu Ala Val Leu Ala Ser  
1 5 10 15

15 Leu Ile Ile Ala Thr Asn Thr Leu Val Ala Val Ala Val Leu Leu Leu  
20 25 30

Ile His Lys Asn Asp Gly Val Ser Leu Cys Phe Thr Leu Asn Leu Ala  
35 40 45

Val Ala Asp Thr Leu Ile Gly Val Ala Ile Ser Gly Leu Leu Thr Asp  
50 55 60

20 Gln Leu Ser Ser Pro Ser Arg Pro Thr Gln Lys Thr Leu Cys Ser Leu  
65 70 75 80

Arg Met Ala Phe Val Thr Ser Ser Ala Ala Ala Ser Val Leu Thr Val  
85 90

Met Leu Ile Thr Phe Asp Arg Tyr Leu Ala Ile Lys Gln Pro Phe Arg  
25 100 105

Tyr Leu Lys Ile Met Ser Gly Phe Val Ala Gly Ala Cys Ile Ala Gly  
115 120

Leu Trp Leu Val Ser Tyr Leu Ile Gly Phe Leu Pro Leu Gly Ile Pro  
120

30 Met Phe Gln Gln Thr Ala Tyr Lys Gly Gln Cys Ser Phe Phe Ala Val  
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

Phe His Pro His Phe Val Leu Thr Leu Ser Cys Val Gly Phe Phe Pro

Ala Met Leu Leu Phe Val Phe Phe Tyr Cys Asp Met Leu Lys Ile Ala

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Ser Met His Ser Gln Gln Ile Arg Lys Met Glu His Ala Gly Ala Met  
195 200 205

Ala Gly Gly Tyr Arg Ser Pro Arg Thr Pro Ser Asp Phe Lys Ala Leu  
210 215 220

|   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 5 | Arg | Thr | Val | Ser | Val | Leu | Ile | Gly | Ser | Phe | Ala | Leu | Ser | Trp | Thr | Pro |
|   | 225 |     |     |     | 230 |     |     |     |     | 235 |     |     |     | 240 |     |     |

Phe Leu Ile Thr Gly Ile Val Gln Val Ala Cys Gln Glu Cys His Leu  
                  245                 250                 255

Tyr Leu Val Leu Glu Arg Tyr Leu Trp Leu Leu Gly Val Gly Asn Ser  
                  260                   265                   270

Leu Leu Asn Pro Leu Ile Tyr Ala Tyr Trp Gln Lys Glu Val Arg Leu  
275 280 285

Gln Leu Tyr His Met Ala Leu Gly Val Lys Lys Val Leu Thr Ser Phe  
290 295 300

15 Leu Leu Phe Leu Ser Ala Arg Asn Cys Gly Pro Glu Arg Pro Arg Glu  
305 310 315 320

Ser Ser Cys His Ile Val Thr Ile Ser Ser Ser Glu Phe Asp Gly  
325 330 335

(10) INFORMATION FOR SEQ ID NO:9:

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1413 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

ATGGACACTA CCATGGAAGC TGACCTGGGT GCCACTGGCC ACAGGGCCCCG CACAGAGCTT 60

GATGATGAGG ACTCCTACCC CCAAGGTGGC TGGGACACGG TCTTCCTGGT GGCCCTGCTG 120

CTCCTTGGGC TGCCAGCCAA TGGGTTGATG GCGTGGCTGG CCGGCTCCCCA GGCCCGGGCAT 180

30 GGAGCTGGCA CGCGTCTGGC GCTGCTCCTG CTCAGCCTGG CCCTCTCTGA CTTCTTGTTC 240

CTGGCAGCAG CGGCCTTCCA GATCCTAGAG ATCCGGCATG GGGGACACTG GCCGCTGGGG 300

ACAGCTGCCT GCCGCTTCTA CTACTTCCTA TGGGGCGTGT CCTACTCCTC CGGCCCTCTTC 360

CTGCTGGCGC CCCTCAGCCT CGACCGCTGC CTGCTGGCGC TGTGCCAACG CTGGTACCCCT 420

GGGCACCGCC CAGTCCGCCT GCCCCCTCTGG GTCTGCGCCG GTGTCTGGGT SCTGGCCACA 480

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CTCTTCAGCG TGCCCTGGCT GGTCTTCCCC GAGGCTGCCG TCTGGTGGTA CGACCTGGTC 540  
 ATCTGCCTGG ACTTCTGGGA CAGCGAGGAG CTGTCGCTGA GGATGCTGGA GGTCCTGGGG 600  
 GGCTTCCTGC CTTTCCTCCT GCTGCTCGTC TGCCACGTGC TCACCCAGGC CACAGCCTGT 660  
 CGCACCTGCC ACCGCCAACA GCAGCCCGCA GCCTGCCGGG GCTTCGCCCG TGTGCCAGG 720  
 5 ACCATTCTGT CAGCCTATGT GGTCTTGAGG CTGCCCTACC AGCTGGCCA GCTGCTCTAC 780  
 CTGGCCTTCC TGTGGGACGT CTACTCTGGC TACCTGCTCT GGGAGGCCCT GGTCTACTCC 840  
 GACTACCTGA TCCTACTCAA CAGCTGCCTC AGCCCCTTCC TCTGCCTCAT GGCCAGTGCC 900  
 GACCTCCGGA CCCTGCTGCG CTCCGTGCTC TCGTCCTTCG CGGCAGCTCT CTGCGAGGAG 960  
 CGGCCGGGCA GCTTCACGCC CACTGAGCCA CAGACCCAGC TAGATTCTGA GGGTCCA1020  
 10 CTGCCAGAGC CGATGGCAGA GGCCCAGTCA CAGATGGATC CTGTGGCCA GCCTCAGGTG1080  
 AACCCCCACAC TCCAGCCACG ATCGGATCCC ACAGCTCAGC CACAGCTGAA CCTACGGCC1140  
 CAGCCACAGT CGGATCCCAC AGCCCAGCCA CAGCTGAACC TCATGGCCA GCCACAGTCA1200  
 GATTCTGTGG CCCAGCCACA GGCAGACACT AACGTCCAGA CCCCTGCACC TGCTGCCAGT1260  
 TCTGTGCCCA GTCCCTGTGA TGAAGCTTCC CCAACCCCAT CCTCGCATCC TACCCCAGGG1320  
 15 GCCCTTGAGG ACCCAGCCAC ACCTCCTGCC TCTGAAGGAG AAAGCCCCAG CAGCACCCCG1380  
 CCAGAGGCCGG CCCCGGGCGC AGGCCCCACG TGA 1413

(ii) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 468 amino acids
- 20 (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

25 Met Asp Thr Thr Met Glu Ala Asp Leu Gly Ala Thr Gly His Arg Pro  
 1 5 10 15  
 Arg Thr Glu Leu Asp Asp Glu Asp Ser Tyr Pro Gln Gly Gly Trp Asp  
 20 25 30  
 30 Thr Val Phe Leu Val Ala Leu Leu Leu Gly Leu Pro Ala Asn Gly  
 35 40 45  
 Leu Met Ala Trp Leu Ala Gly Ser Gln Ala Arg His Gly Ala Gly Thr

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|    | 50                              | 55                              | 60  |     |
|----|---------------------------------|---------------------------------|-----|-----|
|    | Arg Leu Ala Leu Leu Leu Leu Ser | Leu Ala Leu Ser Asp Phe Leu Phe |     |     |
| 65 | 65                              | 70                              | 75  | 80  |
| 5  | Leu Ala Ala Ala Ala Phe Gln Ile | Leu Glu Ile Arg His Gly Gly His |     |     |
|    | 85                              | 90                              | 95  |     |
|    | Trp Pro Leu Gly Thr Ala Ala Cys | Arg Phe Tyr Tyr Phe Leu Trp Gly |     |     |
|    | 100                             | 105                             | 110 |     |
|    | Val Ser Tyr Ser Ser Gly Leu Phe | Leu Leu Ala Ala Leu Ser Leu Asp |     |     |
|    | 115                             | 120                             | 125 |     |
| 10 | Arg Cys Leu Leu Ala Leu Cys Pro | His Trp Tyr Pro Gly His Arg Pro |     |     |
|    | 130                             | 135                             | 140 |     |
|    | Val Arg Leu Pro Leu Trp Val Cys | Ala Gly Val Trp Val Leu Ala Thr |     |     |
|    | 145                             | 150                             | 155 | 160 |
| 15 | Leu Phe Ser Val Pro Trp Leu Val | Phe Pro Glu Ala Ala Val Trp Trp |     |     |
|    | 165                             | 170                             | 175 |     |
|    | Tyr Asp Leu Val Ile Cys Leu Asp | Phe Trp Asp Ser Glu Glu Leu Ser |     |     |
|    | 180                             | 185                             | 190 |     |
|    | Leu Arg Met Leu Glu Val Leu Gly | Gly Phe Leu Pro Phe Leu Leu     |     |     |
|    | 195                             | 200                             | 205 |     |
| 20 | Leu Val Cys His Val Leu Thr Gln | Ala Thr Arg Thr Cys His Arg Gln |     |     |
|    | 210                             | 215                             | 220 |     |
|    | Gln Gln Pro Ala Ala Cys Arg Gly | Phe Ala Arg Val Ala Arg Thr Ile |     |     |
|    | 225                             | 230                             | 235 | 240 |
| 25 | Leu Ser Ala Tyr Val Val Leu Arg | Leu Pro Tyr Gln Leu Ala Gln Leu |     |     |
|    | 245                             | 250                             | 255 |     |
|    | Leu Tyr Leu Ala Phe Leu Trp Asp | Val Tyr Ser Gly Tyr Leu Leu Trp |     |     |
|    | 260                             | 265                             | 270 |     |
|    | Glu Ala Leu Val Tyr Ser Asp Tyr | Leu Ile Leu Leu Asn Ser Cys Leu |     |     |
|    | 275                             | 280                             | 285 |     |
| 30 | Ser Pro Phe Leu Cys Leu Met Ala | Ser Ala Asp Leu Arg Thr Leu Leu |     |     |
|    | 290                             | 295                             | 300 |     |
|    | Arg Ser Val Leu Ser Ser Phe Ala | Ala Ala Leu Cys Glu Glu Arg Pro |     |     |
|    | 305                             | 310                             | 315 | 320 |
| 35 | Gly Ser Phe Thr Pro Thr Glu Pro | Gln Thr Gln Leu Asp Ser Glu Gly |     |     |
|    | 325                             | 330                             | 335 |     |
|    | Pro Thr Leu Pro Glu Pro Met Ala | Glu Ala Gln Ser Gln Met Asp Pro |     |     |
|    | 340                             | 345                             | 350 |     |

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Val Ala Gln Pro Gln Val Asn Pro Thr Leu Gln Pro Arg Ser Asp Pro  
355 360 365

Thr Ala Gln Pro Gln Leu Asn Pro Thr Ala Gln Pro Gln Ser Asp Pro  
370 375 380

5 Thr Ala Gln Pro Gln Leu Asn Leu Met Ala Gln Pro Gln Ser Asp Ser  
385 390 395 400

Val Ala Gln Pro Gln Ala Asp Thr Asn Val Gln Thr Pro Ala Pro Ala  
405 410 415

Ala Ser Ser Val Pro Ser Pro Cys Asp Glu Ala Ser Pro Thr Pro Ser  
420 425 430

Ser His Pro Thr Pro Gly Ala Leu Glu Asp Pro Ala Thr Pro Pro Ala  
435 440 445

Ser Glu Gly Glu Ser Pro Ser Ser Thr Pro Pro Glu Ala Ala Pro Gly  
450 455 460

15 Ala Gly Pro Thr  
465

(12) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1248 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

25 ATGTCAGGG A TGGAAAAACT TCAGAATGCT TCCTGGATCT ACCAGCAGAA ACTAGAAGAT 60  
CCATTCCAGA AACACCTGAA CAGCACCGAG GAGTATCTGG CCTTCCTCTG CGGACCTCGG 120  
CGCAGCCACT TCTTCCTCCC CGTGTCTGTG GTGTATGTGC CAATTTTGT GGTGGGGGTC 180  
ATTGGCAATG TCCTGGTGTG CCTGGTGATT CTGCACCACC AGGCTATGAA GACGCCACC 240  
AACTACTACC TCTTCAGCCT GGCGGTCTCT GACCTCCTGG TCCTGCTCCT TGGAATGCC 300  
30 CTGGAGGTCT ATGAGATGTG GCGCAACTAC CCTTTCTTGT TCGGGCCCCGT GGGCTGCTAC 360  
TTCA~~A~~GACGG CCCTCTTGA GACCGTGTGC TTCGCCTCCA TCCTCAGCAT CACCACCGTC 420  
AGCGTGGAGC GCTACGTGGC CATCCTACAC CCGTTCCGCG CCAAACGTCA GAGCACCCGG 480  
CGCCGGGCC TCAGGGATCCT CGGCATCGTC TGGGGCTTCT CCGTGCTCTT CTCCCTGCC 540

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AACACCAGCA TCCATGGCAT CAAGTTCCAC TACTTCCCCA ATGGGTCCCT GGTCCCAGGT 600  
 TCGGCCACCT GTACGGTCAT CAAGCCCAGT TGGATCTACA ATTTCATCAT CCAGGTCACC 660  
 TCCTTCCTAT TCTACCTCCT CCCCATGACT GTCATCAGTG TCCTCTACTA CCTCATGGCA 720  
 CTCAGACTAA AGAAAAGACAA ATCTCTTGAG GCAGATGAAG GGAATGCAAA TATTCAAAGA 780  
 5 CCCTGCAGAA AATCAGTCAA CAAGATGCTG TTTGTCTGG TCTTAGTGTT TGCTATCTGT 840  
 TGGGCCCCGT TCCACATTGA CCGACTCTTC TTCAGCTTG TGGAGGAGTG GAGTGAATCC 900  
 CTGGCTGCTG TGTCAACCT CGTCCATGTG GTGTCAGGTG TCTTCTTCTA CCTGAGCTCA 960  
 GCTGTCAACC CCATTATCTA TAACCTACTG TCTCGCCGCT TCCAGGCAGC ATTCCAGAA 1020  
 GTGATCTCTT CTTTCCACAA ACAGTGGCAC TCCCAGCATG ACCCACAGTT GCCACCTGCC 1080  
 10 CAGCGGAACA TCTTCCTGAC AGAATGCCAC TTTGTGGAGC TGACCGAAGA TATAGGTCCC 1140  
 CAATTCCCAT GTCAGTCATC CATGCACAAAC TCTCACCTCC CAACAGCCCT CTCTAGTGAA 1200  
 CAGATGTCAA GAACAAACTA TCAAAGCTTC CACTTTAACAA AACCTGA 1248

(13) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 415 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:  
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Met Ser Gly Met Glu Lys Leu Gln Asn Ala Ser Trp Ile Tyr Gln Gln  
 1 5 10 15

Lys Leu Glu Asp Pro Phe Gln Lys His Leu Asn Ser Thr Glu Glu Tyr  
 20 25 30

25 Leu Ala Phe Leu Cys Gly Pro Arg Arg Ser His Phe Phe Leu Pro Val  
 35 40 45

Ser Val Val Tyr Val Pro Ile Phe Val Val Gly Val Ile Gly Asn Val  
 50 55 60

30 Leu Val Cys Leu Val Ile Leu Gln His Gln Ala Met Lys Thr Pro Thr  
 65 70 75 80

Asn Tyr Tyr Leu Phe Ser Leu Ala Val Ser Asp Leu Leu Val Leu Leu  
 85 90 95

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|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Leu | Gly | Met | Pro | Leu | Glu | Val | Tyr | Glu | Met | Trp | Arg | Asn | Tyr | Pro | Phe |
|    |     |     |     |     | 100 |     |     |     | 105 |     |     |     |     |     | 110 |     |
|    | Leu | Phe | Gly | Pro | Val | Gly | Cys | Tyr | Phe | Lys | Thr | Ala | Leu | Phe | Glu | Thr |
|    |     |     |     |     | 115 |     |     |     | 120 |     |     |     |     |     | 125 |     |
| 5  | Val | Cys | Phe | Ala | Ser | Ile | Leu | Ser | Ile | Thr | Thr | Val | Ser | Val | Glu | Arg |
|    |     |     |     |     | 130 |     |     |     | 135 |     |     |     |     |     | 140 |     |
|    | Tyr | Val | Ala | Ile | Leu | His | Pro | Phe | Arg | Ala | Lys | Leu | Gln | Ser | Thr | Arg |
|    |     |     |     |     | 145 |     |     |     | 150 |     |     |     | 155 |     | 160 |     |
| 10 | Arg | Arg | Ala | Leu | Arg | Ile | Leu | Gly | Ile | Val | Trp | Gly | Phe | Ser | Val | Leu |
|    |     |     |     |     | 165 |     |     |     | 170 |     |     |     |     |     | 175 |     |
|    | Phe | Ser | Leu | Pro | Asn | Thr | Ser | Ile | His | Gly | Ile | Lys | Phe | His | Tyr | Phe |
|    |     |     |     |     | 180 |     |     |     | 185 |     |     |     |     |     | 190 |     |
|    | Pro | Asn | Gly | Ser | Leu | Val | Pro | Gly | Ser | Ala | Thr | Cys | Thr | Val | Ile | Lys |
|    |     |     |     |     | 195 |     |     |     | 200 |     |     |     |     |     | 205 |     |
| 15 | Pro | Met | Trp | Ile | Tyr | Asn | Phe | Ile | Ile | Gln | Val | Thr | Ser | Phe | Leu | Phe |
|    |     |     |     |     | 210 |     |     |     | 215 |     |     |     |     |     | 220 |     |
|    | Tyr | Leu | Leu | Pro | Met | Thr | Val | Ile | Ser | Val | Leu | Tyr | Tyr | Leu | Met | Ala |
|    |     |     |     |     | 225 |     |     |     | 230 |     |     |     | 235 |     | 240 |     |
| 20 | Leu | Arg | Leu | Lys | Lys | Asp | Lys | Ser | Leu | Glu | Ala | Asp | Glu | Gly | Asn | Ala |
|    |     |     |     |     | 245 |     |     |     | 250 |     |     |     |     |     | 255 |     |
|    | Asn | Ile | Gln | Arg | Pro | Cys | Arg | Lys | Ser | Val | Asn | Lys | Met | Leu | Phe | Val |
|    |     |     |     |     | 260 |     |     |     | 265 |     |     |     |     |     | 270 |     |
|    | Leu | Val | Leu | Val | Phe | Ala | Ile | Cys | Trp | Ala | Pro | Phe | His | Ile | Asp | Arg |
|    |     |     |     |     | 275 |     |     |     | 280 |     |     |     |     |     | 285 |     |
| 25 | Leu | Phe | Phe | Ser | Phe | Val | Glu | Glu | Trp | Ser | Glu | Ser | Leu | Ala | Ala | Val |
|    |     |     |     |     | 290 |     |     |     | 295 |     |     |     |     |     | 300 |     |
|    | Phe | Asn | Leu | Val | His | Val | Val | Ser | Gly | Val | Phe | Phe | Tyr | Leu | Ser | Ser |
|    |     |     |     |     | 305 |     |     |     | 310 |     |     |     | 315 |     | 320 |     |
| 30 | Ala | Val | Asn | Pro | Ile | Ile | Tyr | Asn | Leu | Leu | Ser | Arg | Arg | Phe | Gln | Ala |
|    |     |     |     |     | 325 |     |     |     | 330 |     |     |     |     |     | 335 |     |
|    | Ala | Phe | Gln | Asn | Val | Ile | Ser | Ser | Phe | His | Lys | Gln | Trp | His | Ser | Gln |
|    |     |     |     |     | 340 |     |     |     | 345 |     |     |     |     |     | 350 |     |
|    | His | Asp | Pro | Gln | Leu | Pro | Pro | Ala | Gln | Arg | Asn | Ile | Phe | Leu | Thr | Glu |
|    |     |     |     |     | 355 |     |     |     | 360 |     |     |     |     |     | 365 |     |
| 35 | Cys | His | Phe | Val | Glu | Leu | Thr | Glu | Asp | Ile | Gly | Pro | Gln | Phe | Pro | Cys |
|    |     |     |     |     | 370 |     |     |     | 375 |     |     |     |     |     | 380 |     |
|    | Gln | Ser | Ser | Met | His | Asn | Ser | His | Leu | Pro | Thr | Ala | Leu | Ser | Ser | Glu |
|    |     |     |     |     | 385 |     |     |     | 390 |     |     |     | 395 |     | 400 |     |

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Gln Met Ser Arg Thr Asn Tyr Gln Ser Phe His Phe Asn Lys Thr  
405 410 415

(14) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 1173 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

ATGCCAGATA CTAATAGCAC AATCAATTAA TCACTAAGCA CTCGTGTTAC TTTAGCATT 60  
TTTATGTCCT TAGTAGCTTT TGCTATAATG CTAGGAAATG CTTTGGTCAT TTTAGCTTTT 120  
GTGGTGGACA AAAACCTTAG ACATCGAAGT AGTTATTTTT TCTTTAACCTT GGCCATCTCT 180  
GACTTCTTG TGGGTGTGAT CTCCATTCCCT TTGTACATCC CTCACACGCT GTTCGAATGG 240  
15 GATTTTGGAA AGGAAATCTG TGTATTTGG CTCACTACTG ACTATCTGTT ATGTACAGCA 300  
TCTGTATATA ACATTGTCCT CATCAGCTAT GATCGATACC TGTCAGTCTC AAATGCTGTG 360  
TCTTATAGAA CTCAACATAC TGGGGCTTG AAGATTGTTA CTCTGATGGT GGCGTTTGG 420  
GTGCTGGCCT TCTTAGTGAA TGGGCCAATG ATTCTAGTTT CAGAGTCTTG GAAGGATGAA 480  
GGTAGTGAAT GTGAACCTGG ATTTTTTCG GAATGGTACA TCCTTGCAT CACATCATTC 540  
20 TTGGAATTG TGATCCCAGT CATCTTAGTC GCTTATTTCA ACATGAATAT TTATTGGAGC 600  
CTGTGGAAGC GTGATCATCT CAGTAGGTGC CAAAGCCATC CTGGACTGAC TGCTGTCTCT 660  
TCCAACATCT GTGGACACTC ATTCAAGAGGT AGACTATCTT CAAGGAGATC TCTTCTGCA 720  
TCGACAGAAG TTCTGCATC CTTTCATTCA GAGAGACAGA GGAGAAAGAG TAGTCTCATG 780  
TTTCCTCAA GAACCAAGAT GAATAGCAAT ACAATTGCTT CCAAAATGGG TTCCTTCTCC 840  
25 CAATCAGATT CTGTAGCTCT TCACCAAAGG GAACATGTTG AACTGCTTAG AGCCAGGAGA 900  
TTAGCCAAGT CACTGGCCAT TCTCTTAGGG GTTTTGCTG TTTGCTGGC TCCATATTCT 960  
CTGTTCACAA TTGTCCTTTC ATTTTATTCC TCAGCAACAG GTCCTAAATC AGTTTGGTAT1020  
AGAATTGCAT TTTGGCTTCA GTGGTTCAAT CCCTTTGTCA ATCCTCTTT GTATCCATTG1080  
TGTCACAAGC GCTTTCAAAA GGCTTCTTG AAAATATTTT GTATAAAAAA GCAACCTCTA1140  
30 CCATCACAAAC ACAGTCGGTC AGTATCTTCT TAA

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## (15) INFORMATION FOR SEQ ID NO:14:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 390 amino acids
- (B) TYPE: amino acid
- 5 (C) STRANDEDNESS:
- (D) TOPOLOGY: not relevant

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

|    |   |
|----|---|
| 10 | Met Pro Asp Thr Asn Ser Thr Ile Asn Leu Ser Leu Ser Thr Arg Val |
|    | 1 5 10 15   |
|    | Thr Leu Ala Phe Phe Met Ser Leu Val Ala Phe Ala Ile Met Leu Gly |
|    | 20 25 30  |
|    | Asn Ala Leu Val Ile Leu Ala Phe Val Val Asp Lys Asn Leu Arg His |
|    | 35 40 45  |
| 15 | Arg Ser Ser Tyr Phe Phe Leu Asn Leu Ala Ile Ser Asp Phe Phe Val |
|    | 50 55 60  |
|    | Gly Val Ile Ser Ile Pro Leu Tyr Ile Pro His Thr Leu Phe Glu Trp |
|    | 65 70 75 80   |
| 20 | Asp Phe Gly Lys Glu Ile Cys Val Phe Trp Leu Thr Thr Asp Tyr Leu |
|    | 85 90 95  |
|    | Leu Cys Thr Ala Ser Val Tyr Asn Ile Val Leu Ile Ser Tyr Asp Arg |
|    | 100 105 110   |
|    | Tyr Leu Ser Val Ser Asn Ala Val Ser Tyr Arg Thr Gln His Thr Gly |
|    | 115 120 125   |
| 25 | Val Leu Lys Ile Val Thr Leu Met Val Ala Val Trp Val Leu Ala Phe |
|    | 130 135 140   |
|    | Leu Val Asn Gly Pro Met Ile Leu Val Ser Glu Ser Trp Lys Asp Glu |
|    | 145 150 155 160   |
| 30 | Gly Ser Glu Cys Glu Pro Gly Phe Phe Ser Glu Trp Tyr Ile Leu Ala |
|    | 165 170 175   |
|    | Ile Thr Ser Phe Leu Glu Phe Val Ile Pro Val Ile Leu Val Ala Tyr |
|    | 180 185 190   |
|    | Phe Asn Met Asn Ile Tyr Trp Ser Leu Trp Lys Arg Asp His Leu Ser |
|    | 195 200 205   |
| 35 | Arg Cys Gln Ser His Pro Gly Leu Thr Ala Val Ser Ser Asn Ile Cys |
|    | 210 215 220   |

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|     |   |     |     |     |
|-----|---|-----|-----|-----|
|     | Gly His Ser Phe Arg Gly Arg Leu Ser Ser Arg Arg Ser Leu Ser Ala |     |     |     |
| 225 | 230   | 235 | 240 |     |
|     | Ser Thr Glu Val Pro Ala Ser Phe His Ser Glu Arg Gln Arg Arg Lys |     |     |     |
| 245 | 250   | 255 |     |     |
| 5   | Ser Ser Leu Met Phe Ser Ser Arg Thr Lys Met Asn Ser Asn Thr Ile |     |     |     |
|     | 260   | 265 | 270 |     |
|     | Ala Ser Lys Met Gly Ser Phe Ser Gln Ser Asp Ser Val Ala Leu His |     |     |     |
|     | 275   | 280 | 285 |     |
| 10  | Gln Arg Glu His Val Glu Leu Leu Arg Ala Arg Arg Leu Ala Lys Ser |     |     |     |
|     | 290   | 295 | 300 |     |
|     | Leu Ala Ile Leu Leu Gly Val Phe Ala Val Cys Trp Ala Pro Tyr Ser |     |     |     |
|     | 305   | 310 | 315 | 320 |
|     | Leu Phe Thr Ile Val Leu Ser Phe Tyr Ser Ser Ala Thr Gly Pro Lys |     |     |     |
|     | 325   | 330 | 335 |     |
| 15  | Ser Val Trp Tyr Arg Ile Ala Phe Trp Leu Gln Trp Phe Asn Ser Phe |     |     |     |
|     | 340   | 345 | 350 |     |
|     | Val Asn Pro Leu Leu Tyr Pro Leu Cys His Lys Arg Phe Gln Lys Ala |     |     |     |
|     | 355   | 360 | 365 |     |
| 20  | Phe Leu Lys Ile Phe Cys Ile Lys Lys Gln Pro Leu Pro Ser Gln His |     |     |     |
|     | 370   | 375 | 380 |     |
|     | Ser Arg Ser Val Ser Ser   |     |     |     |
|     | 385   | 390 |     |     |

(16) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 1128 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

```

ATGGCGAACG CGAGCGAGCC GGGTGGCAGC GGCGGCGGCG AGGCAGGCCG CCTGGGCCTC 60
AAGCTGGCCA CGCTCAGCCT GCTGCTGTGC GTGAGCCTAG CGGGCAACGT GCTGTTGCG 120
CTGCTGATCG TGCGGGAGCG CAGCCTGCAC CGCGCCCCGT ACTACCTGCT GCTCGACCTG 180
TGCCTGGCCG ACGGGCIGCG CGCGCTCGCC TGCCTCCCCT CGTCATGCT GGCGGCGCGG 240
35 CGTGCAGCGG CCGCGGCGGG GGCGCCGCG GGCGCGCTGG GCTGCAAGCT GCTCGCCCTTC 300

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CTGGCCGCGC TCTTCTGCTT CCACGCCGCC TTCCTGCTGC TGGGCGTGGG CGTCACCCGC 360  
 TACCTGGCCA TCGCGCACCA CCGCTTCTAT GCAGAGCGCC TGGCCGGCTG GCCGTGCGCC 420  
 GCCATGCTGG TGTGCGCCGC CTGGCGCTG GCGCTGGCCG CGGCCTTCCC GCCAGTGCTG 480  
 GACGGCGGTG GCGACGACGA GGACGCGCCG TGCGCCCTGG AGCAGCGGCC CGACGGCGCC 540  
 5 CCCGGCGCGC TGGGCTTCCT GCTGCTGCTG GCCGTGGTGG TGGGCGCCAC GCACCTCGTC 600  
 TACCTCCCCC TGCTCTTCTT CATCCACGAC CGCCGCAAGA TGCGGCCCCGC GCGCCTGGTG 660  
 CCCGCCGTCA GCCACGACTG GACCTTCCAC GGCCCGGGCG CCACCGGCCA GGCGGCCGC 720  
 AACTGGACGG CGGGCTTCGG CGCGGGGCC ACGCCGCCCG CGCTTGTGGG CATCCGGCCC 780  
 GCAGGGCCGG GCCGCGGCCGC GCGCCGCCTC CTCGTGCTGG AAGAATTCAA GACGGAGAAG 840  
 10 AGGCTGTGCA AGATGTTCTA CGCCGTCACG CTGCTCTTCC TGCTCCTCTG GGGGCCCTAC 900  
 GTCGTGGCCA GCTACCTGCG GGTCTGGTG CGGCCCCGGCG CCGTCCCCCA GGCTTACCTG 960  
 ACGGCCTCCG TGTGGCTGAC CTTCGCGCAG GCCGGCATCA ACCCCGTCGT GTGCTTCCTC 1020  
 TTCAACAGGG AGCTGAGGGG CTGCTTCAGG GCCCAGTTCC CCTGCTGCCA GAGCCCCCGG 1080  
 ACCACCCAGG CGACCCATCC CTGCGACCTG AAAGGCATTG GTTTATGA 1128

15 (17) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 375 amino acids
- (B) TYPE: amino acid

(C) STRANDEDNESS:

20 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ala | Asn | Ala | Ser | Glu | Pro | Gly | Gly | Ser | Gly | Gly | Gly | Glu | Ala | Ala |
| 1   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     | 10  | 15  |

|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 25 | Ala | Leu | Gly | Leu | Lys | Leu | Ala | Thr | Leu | Ser | Leu | Leu | Leu | Cys | Val | Ser |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     | 20  | 25  | 30  |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |    |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|
| Leu | Ala | Gly | Asn | Val | Leu | Phe | Ala | Leu | Leu | Ile | Val | Arg | Glu | Arg | Ser |    |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |    |
|     |     |     |     |     |     |     |     |     |     |     |     |     |     | 35  | 40  | 45 |

|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 30 | Leu | His | Arg | Ala | Pro | Tyr | Tyr | Leu | Leu | Leu | Asp | Leu | Cys | Leu | Ala | Asp |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     | 50  | 55  | 60  |

|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 65 | Gly | Leu | Arg | Ala | Leu | Ala | Cys | Leu | Pro | Ala | Val | Met | Leu | Ala | Ala | Arg |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     | 70  | 75  | 80  |

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|    |   |     |     |     |
|----|---|-----|-----|-----|
|    | Arg Ala Ala Ala Ala Ala Gly Ala Pro Pro Gly Ala Leu Gly Cys Lys |     |     |     |
|    | 85  | 90  | 95  |     |
|    | Leu Leu Ala Phe Leu Ala Ala Leu Phe Cys Phe His Ala Ala Phe Leu |     |     |     |
|    | 100   | 105 | 110 |     |
| 5  | Leu Leu Gly Val Gly Val Thr Arg Tyr Leu Ala Ile Ala His His Arg |     |     |     |
|    | 115   | 120 | 125 |     |
|    | Phe Tyr Ala Glu Arg Leu Ala Gly Trp Pro Cys Ala Ala Met Leu Val |     |     |     |
|    | 130   | 135 | 140 |     |
| 10 | Cys Ala Ala Trp Ala Leu Ala Leu Ala Ala Phe Pro Pro Val Leu     |     |     |     |
|    | 145   | 150 | 155 | 160 |
|    | Asp Gly Gly Asp Asp Glu Asp Ala Pro Cys Ala Leu Glu Gln Arg     |     |     |     |
|    | 165   | 170 | 175 |     |
|    | Pro Asp Gly Ala Pro Gly Ala Leu Gly Phe Leu Leu Leu Leu Ala Val |     |     |     |
|    | 180   | 185 | 190 |     |
| 15 | Val Val Gly Ala Thr His Leu Val Tyr Leu Arg Leu Leu Phe Phe Ile |     |     |     |
|    | 195   | 200 | 205 |     |
|    | His Asp Arg Arg Lys Met Arg Pro Ala Arg Leu Val Pro Ala Val Ser |     |     |     |
|    | 210   | 215 | 220 |     |
| 20 | His Asp Trp Thr Phe His Gly Pro Gly Ala Thr Gly Gln Ala Ala Ala |     |     |     |
|    | 225   | 230 | 235 | 240 |
|    | Asn Trp Thr Ala Gly Phe Gly Arg Gly Pro Thr Pro Pro Ala Leu Val |     |     |     |
|    | 245   | 250 | 255 |     |
|    | Gly Ile Arg Pro Ala Gly Pro Gly Arg Gly Ala Arg Arg Leu Leu Val |     |     |     |
|    | 260   | 265 | 270 |     |
| 25 | Leu Glu Glu Phe Lys Thr Glu Lys Arg Leu Cys Lys Met Phe Tyr Ala |     |     |     |
|    | 275   | 280 | 285 |     |
|    | Val Thr Leu Leu Phe Leu Leu Leu Trp Gly Pro Tyr Val Val Ala Ser |     |     |     |
|    | 290   | 295 | 300 |     |
| 30 | Tyr Leu Arg Val Leu Val Arg Pro Gly Ala Val Pro Gln Ala Tyr Leu |     |     |     |
|    | 305   | 310 | 315 | 320 |
|    | Thr Ala Ser Val Trp Leu Thr Phe Ala Gln Ala Gly Ile Asn Pro Val |     |     |     |
|    | 325   | 330 | 335 |     |
|    | Val Cys Phe Leu Phe Asn Arg Glu Leu Arg Asp Cys Phe Arg Ala Gln |     |     |     |
|    | 340   | 345 | 350 |     |
| 35 | Phe Pro Cys Cys Gln Ser Pro Arg Thr Thr Gln Ala Thr His Pro Cys |     |     |     |
|    | 355   | 360 | 365 |     |
|    | Asp Leu Lys Gly Ile Gly Leu                                     |     |     |     |

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## (18) INFORMATION FOR SEQ ID NO:17:

## (i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 1002 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

10 ATGAACACCA CAGTGATGCA AGGCTTCAAC AGATCTGAGC GGTGCCAG AGACACTCGG 60  
 ATAGTACAGC TGGTATTCCC AGCCCTCTAC ACAGTGGTTT TCTTGACCGG CATCCTGCTG 120  
 AATACTTTGG CTCTGTGGGT GTTTGTTCAC ATCCCCAGCT CCTCCACCTT CATCATCTAC 180  
 CTCAAAAACA CTTTGGTGGC CGACTTGATA ATGACACTCA TGCTTCCTTT CAAAATCCTC 240  
 TCTGACTCAC ACCTGGCACC CTGGCAGCTC AGAGCTTTG TGTGTCGTTT TTCTTCGGTG 300  
 15 ATATTTTATG AGACCATGTA TGTGGGCATC GTGCTGTTAG GGCTCATAGC CTTTGACAGA 360  
 TTCCTCAAGA TCATCAGACC TTTGAGAAAT ATTTTTCTAA AAAAACCTGT TTTTGCAAAA 420  
 ACGGTCTCAA TCTTCATCTG GTTCTTTTG TTCTTCATCT CCCTGCCAAA TAGGATCTTG 480  
 AGCAACAAGG AAGCAACACC ATCGTCTGTG AAAAAGTGTG CTTCCCTAAA GGGGCCTCTG 540  
 GGGCTGAAAT GGCACTAAAT GGTAAATAAC ATATGCCAGT TTATTTCTG GACTGTTTT 600  
 20 ATCCTAATGC TTGTGTTTA TGTGGTTATT GCAAAAAAAG TATATGATTC TTATAGAAAG 660  
 TCCAAAAGTA AGGACAGAAA AAACAACAAA AAGCTGGAAG GCAAAAGTATT TGTTGTCGTG 720  
 GCTGTCTTCT TTGTGTGTIT TGCTCCATTT CATTGACCA GAGTTCCATA TACTCACAGT 780  
 CAAACCAACA ATAAGACTGA CTGTAGACTG CAAAATCAAC TGTTTATTGC TAAAGAAACA 840  
 ACTCTCTTT TGGCAGCAAC TAACATTGT ATGGATCCCT TAATATACAT ATTCTTATGT 900  
 25 AAAAATTCA CAGAAAAGCT ACCATGTATG CAAGGGAGAA AGACCACAGC ATCAAGCCAA 960  
 GAAAATCATA GCAGTCAGAC AGACAAACATA ACCTTAGGCT GA 1002

## (19) INFORMATION FOR SEQ ID NO:18:

## (i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 233 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:

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(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

|    |   |     |     |     |
|----|---|-----|-----|-----|
|    | Met Asn Thr Thr Val Met Gln Gly Phe Asn Arg Ser Glu Arg Cys Pro |     |     |     |
| 5  | 1   | 5   | 10  | 15  |
|    | Arg Asp Thr Arg Ile Val Gln Leu Val Phe Pro Ala Leu Tyr Thr Val |     |     |     |
|    | 20  | 25  | 30  |     |
|    | Val Phe Leu Thr Gly Ile Leu Leu Asn Thr Leu Ala Leu Trp Val Phe |     |     |     |
|    | 35  | 40  | 45  |     |
| 10 | Val His Ile Pro Ser Ser Ser Thr Phe Ile Ile Tyr Leu Lys Asn Thr |     |     |     |
|    | 50  | 55  | 60  |     |
|    | Leu Val Ala Asp Leu Ile Met Thr Leu Met Leu Pro Phe Lys Ile Leu |     |     |     |
|    | 65  | 70  | 75  | 80  |
| 15 | Ser Asp Ser His Leu Ala Pro Trp Gln Leu Arg Ala Phe Val Cys Arg |     |     |     |
|    | 85  | 90  | 95  |     |
|    | Phe Ser Ser Val Ile Phe Tyr Glu Thr Met Tyr Val Gly Ile Val Leu |     |     |     |
|    | 100   | 105 | 110 |     |
|    | Leu Gly Leu Ile Ala Phe Asp Arg Phe Leu Lys Ile Ile Arg Pro Leu |     |     |     |
|    | 115   | 120 | 125 |     |
| 20 | Arg Asn Ile Phe Leu Lys Lys Pro Val Phe Ala Lys Thr Val Ser Ile |     |     |     |
|    | 130   | 135 | 140 |     |
|    | Phe Ile Trp Phe Phe Leu Phe Phe Ile Ser Leu Pro Asn Thr Ile Leu |     |     |     |
|    | 145   | 150 | 155 | 160 |
| 25 | Ser Asn Lys Glu Ala Thr Pro Ser Ser Val Lys Lys Cys Ala Ser Leu |     |     |     |
|    | 165   | 170 | 175 |     |
|    | Lys Gly Pro Leu Gly Leu Lys Trp His Gln Met Val Asn Asn Ile Cys |     |     |     |
|    | 180   | 185 | 190 |     |
|    | Gln Phe Ile Phe Trp Thr Val Phe Ile Leu Met Leu Val Phe Tyr Val |     |     |     |
|    | 195   | 200 | 205 |     |
| 30 | Val Ile Ala Lys Lys Val Tyr Asp Ser Tyr Arg Lys Ser Lys Ser Lys |     |     |     |
|    | 210   | 215 | 220 |     |
|    | Asp Arg Lys Asn Asn Lys Lys Leu Glu Gly Lys Val Phe Val Val Val |     |     |     |
|    | 225   | 230 | 235 | 240 |
| 35 | Ala Val Phe Phe Val Cys Phe Ala Pro Phe His Phe Ala Arg Val Pro |     |     |     |
|    | 245   | 250 | 255 |     |

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Tyr Thr His Ser Gln Thr Asn Asn Lys Thr Asp Cys Arg Leu Gln Asn  
 260 265 270

Gln Leu Phe Ile Ala Lys Glu Thr Thr Leu Phe Leu Ala Ala Thr Asn  
 275 280 285

5 Ile Cys Met Asp Pro Leu Ile Tyr Ile Phe Leu Cys Lys Lys Phe Thr  
 290 295 300

Glu Lys Leu Pro Cys Met Gln Gly Arg Lys Thr Thr Ala Ser Ser Gln  
 305 310 315 320

10 Glu Asn His Ser Ser Gln Thr Asp Asn Ile Thr Leu Gly  
 325 330

(20) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1122 base pairs
- (B) TYPE: nucleic acid
- 15 (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

ATGGCCAACA CTACCGGAGA GCCTGAGGAG GTGAGCGGGCG CTCTGTCCCC ACCGTCCGCA 60  
 20 TCAGCTTATG TGAAGCTGGT ACTGCTGGG A CTGATTATGT GCGTGAGCCT GGCGGGTAAC 120  
 GCCATCTTGT CCCTGCTGGT GCTCAAGGAG CGTGCCTGC ACAAGGCTCC TTACTACTTC 180  
 CTGCTGGACC TGTGCTGGC CGATGGCATA CGCTCTGCCG TCTGCTTCCC CTTTGTGCTG 240  
 GCTTCTGTGC GCCACGGCTC TTCATGGACC TTCAAGTGCAC TCAGCTGCAA GATTGTGGCC 300  
 TTTATGGCCG TGCTCTTTG CTTCCATGCG GCCTTCATGC TGTTCTGCAT CAGCGTCACC 360  
 25 CGCTACATGG CCATGCCCA CCACCGCTTC TACGCCAACG GCATGACACT CTGGACATGC 420  
 GCGGCTGTCA TCTGCATGGC CTGGACCTG TCTGTGCCA TGGCCTTCCC ACCTGTCTTT 480  
 GACGTGGGCA CCTACAAGTT TATTCGGGAG GAGGACCAAGT GCATCTTGA GCATCGCTAC 540  
 TTCAAGGCCA ATGACACGCT GGGCTTCATG CTTATGTTGG CTGTGCTCAT GGCAGCTACC 600  
 CATGCTGTCT ACGGCAAGCT GCTCCTCTTC GAGTATCGTC ACCGCAAGAT GAAGCCAGTG 660  
 30 CAGATGGTGC CAGCCATCAG CCAGAACTGG ACATTCCATG GTCCCGGGC CACCGGCCAG 720  
 GCTGCTGCCA ACTGGATCGC CGGCTTTGGC CGTGGGCCA TGCCACCAAC CCTGCTGGGT 780  
 ATCCGGCAGA ATGGGCATGC AGCCAGCCGG CGGCTACTGG GCATGGACGA GGTCAAGGGT 840

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GAAAAGCAGC TGGGCCGCAT GTTCTACGCG ATCACACTGC TCTTTCTGCT CCTCTGGTCA 900  
 CCCTACATCG TGGCCTGCTA CTGGCGAGTG TTTGTGAAAG CCTGTGCTGT GCCCCACCGC 960  
 TACCTGGCCA CTGCTGTTG GATGAGCTTC GCCCAGGCTG CCGTCAACCC AATTGTCTGC1020  
 TTCCTGCTCA ACAAGGACCT CAAGAAGTGC CTGACCACTC ACGCCCCCTG CTGGGGCAC1080  
 5 GGAGGTGCC CGGCTCCCAG AGAACCTAC TGTGTCATGT GA 1122

## (21) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 373 amino acids  
 (B) TYPE: amino acid  
 10 (C) STRANDEDNESS:  
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

|    |   |     |     |     |
|----|---|-----|-----|-----|
|    | Met Ala Asn Thr Thr Gly Glu Pro Glu Glu Val Ser Gly Ala Leu Ser |     |     |     |
| 15 | 1   | 5   | 10  | 15  |
|    | Pro Pro Ser Ala Ser Ala Tyr Val Lys Leu Val Leu Leu Gly Leu Ile |     |     |     |
|    | 20  | 25  | 30  |     |
|    | Met Cys Val Ser Leu Ala Gly Asn Ala Ile Leu Ser Leu Leu Val Leu |     |     |     |
|    | 35  | 40  | 45  |     |
| 20 | Lys Glu Arg Ala Leu His Lys Ala Pro Tyr Tyr Phe Leu Leu Asp Leu |     |     |     |
|    | 50  | 55  | 60  |     |
|    | Cys Leu Ala Asp Gly Ile Arg Ser Ala Val Cys Phe Pro Phe Val Leu |     |     |     |
|    | 65  | 70  | 75  | 80  |
| 25 | Ala Ser Val Arg His Gly Ser Ser Trp Thr Phe Ser Ala Leu Ser Cys |     |     |     |
|    | 85  | 90  | 95  |     |
|    | Lys Ile Val Ala Phe Met Ala Val Leu Phe Cys Phe His Ala Ala Phe |     |     |     |
|    | 100   | 105 | 110 |     |
|    | Met Leu Phe Cys Ile Ser Val Thr Arg Tyr Met Ala Ile Ala His His |     |     |     |
|    | 115   | 120 | 125 |     |
| 30 | Arg Phe Tyr Ala Lys Arg Met Thr Leu Trp Thr Cys Ala Ala Val Ile |     |     |     |
|    | 130   | 135 | 140 |     |
|    | Cys Met Ala Trp Thr Leu Ser Val Ala Met Ala Phe Pro Pro Val Phe |     |     |     |
|    | 145   | 150 | 155 | 160 |
| 35 | Asp Val Gly Thr Tyr Lys .he Ile Arg Glu Glu Asp Gln Cys Ile Phe |     |     |     |
|    | 165   | 170 | 175 |     |

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|    |   |
|----|---|
|    | Glu His Arg Tyr Phe Lys Ala Asn Asp Thr Leu Gly Phe Met Leu Met   |
|    | 180   185                                   190                                       |
|    | Leu Ala Val Leu Met Ala Ala Thr His Ala Val Tyr Gly Lys Leu Leu   |
|    | 195   200                                   205                                       |
| 5  | Leu Phe Glu Tyr Arg His Arg Lys Met Lys Pro Val Gin Met Val Pro   |
|    | 210   215                                   220                                       |
|    | Ala Ile Ser Gln Asn Trp Thr Phe His Gly Pro Gly Ala Thr Gly Gln   |
|    | 225   230                                   235                                   240 |
| 10 | Ala Ala Ala Asn Trp Ile Ala Gly Phe Gly Arg Gly Pro Met Pro Pro   |
|    | 245   250                                   255                                       |
|    | Thr Leu Leu Gly Ile Arg Gln Asn Gly His Ala Ala Ser Arg Arg Leu   |
|    | 260   265                                   270                                       |
|    | Leu Gly Met Asp Glu Val Lys Gly Glu Lys Gln Leu Gly Arg Met Phe   |
|    | 275   280                                   285                                       |
| 15 | Tyr Ala Ile Thr Leu Leu Phe Leu Leu Leu Trp Ser Pro Tyr Ile Val   |
|    | 290   295                                   300                                       |
|    | Ala Cys Tyr Trp Arg Val Phe Val Lys Ala Cys Ala Val Pro His Arg   |
|    | 305   310                                   315                                   320 |
| 20 | Tyr Leu Ala Thr Ala Val Trp Met Ser Phe Ala Gln Ala Ala Val Asn   |
|    | 325   330                                   335                                       |
|    | Pro Ile Val Cys Phe Leu Leu Asn Lys Asp Leu Lys Lys Cys Leu Thr   |
|    | 340   345                                   350                                       |
|    | Thr His Ala Pro Cys Trp Gly Thr Gly Gly Ala Pro Ala Pro Arg Glu   |
|    | 355   360                                   365                                       |
| 25 | Pro Tyr Cys Val Met   |
|    | 370   |

## (22) INFORMATION FOR SEQ ID NO:21:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1053 base pairs
- 30 (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

35 ATGGCTTGG AACAGAACCA GTCAACAGAT TATTATTATG AGGAATATGA AATGAATGGC 60  
 ACTTATGACT ACAGTCATA TGAATTGATC TGTATCAAAG AAGATGTCAG AGAATTGCA 120

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AAAGTTTCC TCCCTGTATT CCTCACATA GCTTCGTCA TTGGACTTGC AGGCAATTCC 180  
 ATGGTAGTGG CAATTTATGC CTATTACAAG AACAGAGAA CCAAAACAGA TGTGTACATC 240  
 CTGAATTTGG CTGTAGCAGA TTTACTCCTT CTATTCACTC TGCCCTTTG GGCTGTTAAT 300  
 GCAGTTCATG GGTGGGTTTT AGGGAAAATA ATGTGAAAAA TAACTTCAGC CTTGTACACA 360  
 5 CTAAACTTTG TCTCTGGAAT GCAGTTCTG GCTTGCATCA GCATAGACAG ATATGTGGCA 420  
 GTAACTAATG TCCCCAGCCA ATCAGGAGTG GGAAAACCAT GCTGGATCAT CTGTTCTGT 480  
 GTCTGGATGG CTGCCATCTT GCTGAGCATA CCCCAGCTGG TTTTTATAC AGTAAATGAC 540  
 AATGCTAGGT GCATTCCCAT TTTCCCCGC TACCTAGGAA CATCAATGAA AGCATTGATT 600  
 CAAATGCTAG AGATCTGCAT TGGATTTGTA GTACCCTTTC TTATTATGGG GGTGTGCTAC 660  
 10 TTTATCACGG CAAGGACACT CATGAAGATG CCAAACATTA AAATATCTCG ACCCCTAAAAA 720  
 GTTCTGCTCA CAGTCGTTAT AGTTTCATT GTCACTCAAC TGCCCTATAA CATTGTCAAG 780  
 TTCTGCCGAG CCATAGACAT CATCTACTCC CTGATCACCA GCTGCAACAT GAGCAAACGC 840  
 ATGGACATCG CCATCCAAGT CACAGAAAGC ATTGCACTCT TTCACAGCTG CCTCAACCCA 900  
 ATCCTTTATG TTTTTATGGG AGCATCTTTC AAAAACTACG TTATGAAAGT GGCCAAGAAA 960  
 15 TATGGGTCTT GGAGAAGACA GAGACAAAGT GTGGAGGAGT TTCCCTTTGA TTCTGAGGGT1020  
 CCTACAGAGC CAACCAGTAC TTTAGCATT TAA 1053

(23) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

- 20 (A) LENGTH: 350 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

25 Met Ala Leu Glu Gln Asn Gln Ser Thr Asp Tyr Tyr Tyr Glu Glu Asn  
 1 5 10 15

Glu Met Asn Gly Thr Tyr Asp Tyr Ser Gln Tyr Glu Leu Ile Cys Ile  
 20 25 30

30 Lys Glu Asp Val Arg Glu Phe Ala Lys Val Phe Leu Pro Val Phe Leu  
 35 40 45

Thr Ile Ala Phe Val Ile Gly Leu Ala Gly Asn Ser Met Val Val Ala

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|    |   |   |     |
|----|---|---|-----|
|    | 50  | 55  | 60  |
|    | Ile Tyr Ala Tyr Tyr Lys Lys Gln Arg Thr Lys Thr Asp Val Tyr Ile |   |     |
| 65 | 65  | 70  | 75  |
| 5  | Leu Asn Leu Ala Val Ala Asp Leu Leu Leu Phe Thr Leu Pro Phe     |   |     |
|    | 85  | 90  | 95  |
|    | Trp Ala Val Asn Ala Val His Gly Trp Val Leu Gly Lys Ile Met Cys |   |     |
|    | 100   | 105   | 110 |
|    | Lys Ile Thr Ser Ala Leu Tyr Thr Leu Asn Phe Val Ser Gly Met Gln |   |     |
|    | 115   | 120   | 125 |
| 10 | Phe Leu Ala Cys Ile Ser Ile Asp Arg Tyr Val Ala Val Thr Asn Val |   |     |
|    | 130   | 135   | 140 |
|    | Pro Ser Gln Ser Gly Val Gly Lys Pro Cys Trp Ile Ile Cys Phe Cys |   |     |
|    | 145   | 150   | 155 |
| 15 | 160   | Val Trp Met Ala Ala Ile Leu Leu Ser Ile Pro Gln Leu Val Phe Tyr |     |
|    | 165   | 170   | 175 |
|    | Thr Val Asn Asp Asn Ala Arg Cys Ile Pro Ile Phe Pro Arg Tyr Leu |   |     |
|    | 180   | 185   | 190 |
|    | Gly Thr Ser Met Lys Ala Leu Ile Gln Met Leu Glu Ile Cys Ile Gly |   |     |
|    | 195   | 200   | 205 |
| 20 | Phe Val Val Pro Phe Leu Ile Met Gly Val Cys Tyr Phe Ile Thr Ala |   |     |
|    | 210   | 215   | 220 |
|    | Arg Thr Leu Met Lys Met Pro Asn Ile Lys Ile Ser Arg Pro Leu Lys |   |     |
|    | 225   | 230   | 235 |
| 25 | 240   | Val Leu Leu Thr Val Val Ile Val Phe Ile Val Thr Gln Leu Pro Tyr |     |
|    | 245   | 250   | 255 |
|    | Asn Ile Val Lys Phe Cys Arg Ala Ile Asp Ile Ile Tyr Ser Leu Ile |   |     |
|    | 260   | 265   | 270 |
|    | Thr Ser Cys Asn Met Ser Lys Arg Met Asp Ile Ala Ile Gln Val Thr |   |     |
|    | 275   | 280   | 285 |
| 30 | Glu Ser Ile Ala Leu Phe His Ser Cys Leu Asn Pro Ile Leu Tyr Val |   |     |
|    | 290   | 295   | 300 |
|    | Phe Met Gly Ala Ser Phe Lys Asn Tyr Val Met Lys Val Ala Lys Lys |   |     |
|    | 305   | 310   | 315 |
| 35 | 320   | Tyr Gly Ser Trp Arg Arg Gln Arg Gln Ser Val Glu Glu Phe Pro Phe |     |
|    | 325   | 330   | 335 |
|    | Asp Ser Glu Gly Pro Thr Glu Pro Thr Ser Thr Phe Ser Ile         |   |     |
|    | 340   | 345   | 350 |

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## (24) INFORMATION FOR SEQ ID NO:23:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1116 base pairs
- (B) TYPE: nucleic acid
- 5 (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

ATGCCAGGAA ACGCCACCCC AGTGACCACC ACTGCCCCGT GGGCCTCCCT GGGCCTCTCC . 60  
 10 GCCAAGACCT GCAACAACGT GTCCTTCGAA GAGAGCAGGA TAGTCCTGGT CGTGGTGTAC 120  
 AGCGCGGTGT GCACGCTGGG GGTGCCGGCC AACTGCCTGA CTGCGTGGCT GGCGCTGCTG 180  
 CAGGTACTGC AGGGCAACGT GCTGGCCGTC TACCTGCTCT GCCTGGCACT CTGCGAACTG 240  
 CTGTACACAG GCACGCTGCC ACTCTGGGTC ATCTATATCC GCAACCAGCA CCGCTGGACC 300  
 CTAGGCCTGC TGGCCTCGAA GGTGACCGCC TACATCTTCT TCTGCAACAT CTACGTCAGC 360  
 15 ATCCCTTTCC TGTGCTGCAT CTCCCTGCGAC CGCTTCGTGG CCGTGGTGTAA CGCGCTGGAG 420  
 AGTCGGGGCC GCCGCCGCCG GAGGACCGCC ATCCTCATCT CCGCCTGCAT CTTCATCCTC 480  
 GTCGGGATCG TTCACTACCC GGTGTTCCAG ACGGAAGACA AGGAGACCTG CTTTGACATG 540  
 CTGCAGATGG ACAGCAGGAT TGCCGGGTAC TACTACGCCA GGTCACCGT TGGCTTGCC 600  
 ATCCCTCTCT CCATCATCGC CTTCACCAAAC CACCGGATTTC TCAGGAGCAT CAAGCAGAGC 660  
 20 ATGGGCTTAA GCGCTGCCA GAAGGCCAAG GTGAAGCAGT CGGCCATCGC GGTGGTTGTC 720  
 ATCTTCCTAG TCTGCTTCGC CCCGTACCAAC CTGGTTCTCC TCGTCAAAGC CGCTGCCTTT 780  
 TCCTACTACA GAGGAGACAG GAACGCCATG TGCGGCTTGG AGGAAAGGCT GTACACAGCC 840  
 TCTGTGGTGT TTCTGTGCCT GTCCACGGTG AACGGCGTGG CTGACCCCAT TATCTACGTG 900  
 CTGGCCACGG ACCATTCCCG CCAAGAAGTG TCCAGAAATCC ATAAGGGGTG GAAAGAGTGG 960  
 25 TCCATGAAGA CAGACGTCAC CAGGCTCACC CACAGCAGGG ACACCGAGGA GCTGCAGTCG1020  
 CCCGTGGCCC TTGCAGACCA CTACACCTTC TCCAGGCCCG TGCACCCACC AGGGTCACCA1080  
 TGCCCTGCAA AGAGGCTGAT TGAGGAGTCC TGCTGA 1116

## (25) INFORMATION FOR SEQ ID NO:24:

## (i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 371 amino acids

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- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Met Pro Gly Asn Ala Thr Pro Val Thr Thr Thr Ala Pro Trp Ala Ser  
1 5 10 15

Leu Gly Leu Ser Ala Lys Thr Cys Asn Asn Val Ser Phe Glu Glu Ser  
20 25 30

10 Arg Ile Val Leu Val Val Val Tyr Ser Ala Val Cys Thr Leu Gly Val  
35 40 45

Pro Ala Asn Cys Leu Thr Ala Trp Leu Ala Leu Leu Gln Val Leu Gln  
50 55 60

15 Gly Asn Val Leu Ala Val Tyr Leu Leu Cys Leu Ala Leu Cys Glu Leu  
65 70 75 80

Leu Tyr Thr Gly Thr Leu Pro Leu Trp Val Ile Tyr Ile Arg Asn Gln  
85 90 95

His Arg Trp Thr Leu Gly Leu Leu Ala Ser Lys Val Thr Ala Tyr Ile  
100 105 110

20 Phe Phe Cys Asn Ile Tyr Val Ser Ile Leu Phe Leu Cys Cys Ile Ser  
115 120 125

Cys Asp Arg Phe Val Ala Val Val Tyr Ala Leu Glu Ser Arg Gly Arg  
130 135 140

25 Arg Arg Arg Arg Thr Ala Ile Leu Ile Ser Ala Cys Ile Phe Ile Leu  
145 150 155 160

Val Gly Ile Val His Tyr Pro Val Phe Gln Thr Glu Asp Lys Glu Thr  
165 170 175

Cys Phe Asp Met Leu Gln Met Asp Ser Arg Ile Ala Gly Tyr Tyr Tyr  
180 185 190

30 Ala Arg Phe Thr Val Gly Phe Ala Ile Pro Leu Ser Ile Ile Ala Phe  
195 200 205

Thr Asn His Arg Ile Phe Arg Ser Ile Lys Gln Ser Met Gly Leu Ser  
210 215 220

35 Ala Ala Gln Lys Ala Lys Val Lys His Ser Ala Ile Ala Val Val Val  
225 230 235 240

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|    |   |     |     |
|----|---|-----|-----|
|    | Ile Phe Leu Val Cys Phe Ala Pro Tyr His Leu Val Leu Leu Val Lys |     |     |
|    | 245   | 250 | 255 |
|    | Ala Ala Ala Phe Ser Tyr Tyr Arg Gly Asp Arg Asn Ala Met Cys Gly |     |     |
|    | 260   | 265 | 270 |
| 5  | Leu Glu Glu Arg Leu Tyr Thr Ala Ser Val Val Phe Leu Cys Leu Ser |     |     |
|    | 275   | 280 | 285 |
|    | Thr Val Asn Gly Val Ala Asp Pro Ile Ile Tyr Val Leu Ala Thr Asp |     |     |
|    | 290   | 295 | 300 |
| 10 | His Ser Arg Gln Glu Val Ser Arg Ile His Lys Gly Trp Lys Glu Trp |     |     |
|    | 305   | 310 | 315 |
|    | Ser Met Lys Thr Asp Val Thr Arg Leu Thr His Ser Arg Asp Thr Glu |     |     |
|    | 325   | 330 | 335 |
|    | Glu Leu Gin Ser Pro Val Ala Leu Ala Asp His Tyr Thr Phe Ser Arg |     |     |
|    | 340   | 345 | 350 |
| 15 | Pro Val His Pro Pro Gly Ser Pro Cys Pro Ala Lys Arg Leu Ile Glu |     |     |
|    | 355   | 360 | 365 |
|    | Glu Ser Cys   |     |     |
|    | 370   |     |     |

## (26) INFORMATION FOR SEQ ID NO:25:

20 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1113 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: DNA (genomic)

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

```

ATGGCGAACT ATAGCCATGC AGCTGACAAC ATTTTGCAAA ATCTCTGCC TCTAACAGCC 60
TTTCTGAAAC TGACTTCCTT GGGTTTCATA ATAGGAGTCA GCGTGGTGGG CAACCTCCTG 120
ATCTCCATTG TGCTAGTGAA AGATAAGACC TTGCATAGAG CACCTTACTA CTTCCTGTTG 180
30 GATCTTGCT GTTCAGATAT CCTCAGATCT GCAATTGTT TCCCATTGTG GTTCAACTCT 240
GTCAAAAATG GCTCTACCTG GACTTATGGG ACTCTGACTT GCAAAGTGAT TGCCTTTCTG 300
GGGGTTTGT CCTGTTCCA CACTGCTTTC ATGCTCTTCT GCATCAGTGT CACCAAGATAC 360
TTAGCTATCG CCCATCACCG CTTCTATACA AAGAGGCTGA CCTTTGGAC GTGTCTGGCT 420
GTGATCTGTA TGGTGTGGAC TCTGTCTGTG GCCATGGCAT TTCCCCGGT TTTAGACGTG 480

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GGCACTTACT CATTCAATTAG GGAGGAAGAT CAATGCACCT TCCAACACCG CTCCTTCAGG 540  
 GCTAATGATT CCTTAGGATT TATGCTGCTT CTTGCTCTCA TCCTCCTAGC CACACAGCTT 600  
 GTCTACCTCA AGCTGATATT TTTCGTCCAC GATCGAAGAA AAATGAAGCC AGTCCAGTTT 660  
 GTAGCAGCAG TCAGCCAGAA CTGGACTTTT CATGGTCCTG GAGCCAGTGG CCAGGCAGCT 720  
 5 GCCAATTGGC TAGCAGGATT TGGAAGGGT CCCACACCAC CCACCTTGCT GGGCATCAGG 780  
 CAAAATGCAA ACACCACAGG CAGAAGAAGG CTATTGGTCT TAGACGAGTT CAAAATGGAG 840  
 AAAAGAACATCA GCAGAATGTT CTATATAATG ACTTTTCTGT TTCTAACCTT GTGGGGCCCC 900  
 TACCTGGTGG CCTGTTATTG GAGAGTTTT GCAAGAGGGC CTGTAGTACC AGGGGGATT 960  
 CTAACAGCTG CTGTCTGGAT GAGTTTGCC CAAGCAGGAA TCAATCCTTT TGTCTGCATT1020  
 10 TTCTCAAACA GGGAGCTGAG GCGCTGTTTC AGCACAACCC TTCTTACTG CAGAAAATCC1080  
 AGGTTACCAA GGGAACCTTA CTGTGTTATA TGA 1113

## (27) INFORMATION FOR SEQ ID NO:26:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 370 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS:
  - (D) TOPOLOGY: not relevant
- (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

|    |   |    |    |    |
|----|---|----|----|----|
| 20 | Met Ala Asn Tyr Ser His Ala Ala Asp Asn Ile Leu Gln Asn Leu Ser |    |    |    |
|    | 1   | 5  | 10 | 15 |
|    | Pro Leu Thr Ala Phe Leu Lys Leu Thr Ser Leu Gly Phe Ile Ile Gly |    |    |    |
|    | 20  | 25 | 30 |    |
| 25 | Val Ser Val Val Gly Asn Leu Leu Ile Ser Ile Leu Leu Val Lys Asp |    |    |    |
|    | 35  | 40 | 45 |    |
|    | Lys Thr Leu His Arg Ala Pro Tyr Tyr Phe Leu Leu Asp Leu Cys Cys |    |    |    |
|    | 50  | 55 | 60 |    |
|    | Ser Asp Ile Leu Arg Ser Ala Ile Cys Phe Pro Phe Val Phe Asn Ser |    |    |    |
|    | 65  | 70 | 75 | 80 |
| 30 | Val Lys Asn Gly Ser Thr Trp Thr Tyr Gly Thr Leu Thr Cys Lys Val |    |    |    |
|    | 85  | 90 | 95 |    |
|    | Ile Ala Phe Leu Gly Val Leu Ser Cys The His Thr Ala Phe Met Leu |    |    |    |

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|    | 100   | 105 | 110 |
|----|---|-----|-----|
|    | Phe Cys Ile Ser Val Thr Arg Tyr Leu Ala Ile Ala His His Arg Phe |     |     |
|    | 115   | 120 | 125 |
|    | Tyr Thr Lys Arg Leu Thr Phe Trp Thr Cys Leu Ala Val Ile Cys Met |     |     |
| 5  | 130   | 135 | 140 |
|    | Val Trp Thr Leu Ser Val Ala Met Ala Phe Pro Pro Val Leu Asp Val |     |     |
|    | 145   | 150 | 155 |
|    | Gly Thr Tyr Ser Phe Ile Arg Glu Glu Asp Gln Cys Thr Phe Gln His |     |     |
|    | 165   | 170 | 175 |
| 10 | Arg Ser Phe Arg Ala Asn Asp Ser Leu Gly Phe Met Leu Leu Leu Ala |     |     |
|    | 180   | 185 | 190 |
|    | Leu Ile Leu Leu Ala Thr Gln Leu Val Tyr Leu Lys Leu Ile Phe Phe |     |     |
|    | 195   | 200 | 205 |
| 15 | Val His Asp Arg Arg Lys Met Lys Pro Val Gln Phe Val Ala Ala Val |     |     |
|    | 210   | 215 | 220 |
|    | Ser Gln Asn Trp Thr Phe His Gly Pro Gly Ala Ser Gly Gln Ala Ala |     |     |
|    | 225   | 230 | 235 |
|    | Ala Asn Trp Leu Ala Gly Phe Gly Arg Gly Pro Thr Pro Pro Thr Leu |     |     |
|    | 245   | 250 | 255 |
| 20 | Leu Gly Ile Arg Gln Asn Ala Asn Thr Thr Gly Arg Arg Arg Leu Leu |     |     |
|    | 260   | 265 | 270 |
|    | Val Leu Asp Glu Phe Lys Met Glu Lys Arg Ile Ser Arg Met Phe Tyr |     |     |
|    | 275   | 280 | 285 |
| 25 | Ile Met Thr Phe Leu Phe Leu Thr Leu Trp Gly Pro Tyr Leu Val Ala |     |     |
|    | 290   | 295 | 300 |
|    | Cys Tyr Trp Arg Val Phe Ala Arg Gly Pro Val Val Pro Gly Gly Phe |     |     |
|    | 305   | 310 | 315 |
|    | Leu Thr Ala Ala Val Trp Met Ser Phe Ala Gln Ala Gly Ile Asn Pro |     |     |
|    | 325   | 330 | 335 |
| 30 | Phe Val Cys Ile Phe Ser Asn Arg Glu Leu Arg Arg Cys Phe Ser Thr |     |     |
|    | 340   | 345 | 350 |
|    | Thr Leu Leu Tyr Cys Arg Lys Ser Arg Leu Pro Arg Glu Pro Tyr Cys |     |     |
|    | 355   | 360 | 365 |
| 35 | Val Ile   |     |     |
|    | 370   |     |     |

(28) INFORMATION FOR SEQ ID NO:27:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1080 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

ATGCAGGTCC CGAACAGCAC CGGCCGGAC AACGCGACGC TGCAGATGCT GCGGAACCCG 60  
 GCGATCGCGG TGGCCCTGCC CGTGGTGTAC TCGCTGGTGG CGGCGGTCAAG CATCCCAGGC 120  
 10 AACCTCTTCT CTCTGTGGGT GCTGTGCCGG CGCATGGGC CCAGATCCCC GTCGGTAC 180  
 TTCATGATCA ACCTGAGCGT CACGGACCTG ATGCTGGCCA GCGTGTGTTGCC TTTCAAATC 240  
 TACTACCATT GCAACCGCCA CCACTGGTA TTCGGGGTGC TGCTTGCAA CGTGGTGACC 300  
 GTGGCCTTTT ACGCAAACAT GTATTCCAGC ATCCTCACCA TGACCTGTAT CAGCGTGGAG 360  
 CGCTTCCTGG GGGTCCTGTA CCCGCTCAGC TCCAAGCGCT GGCGCCGCCG TCGTTACGCG 420  
 15 GTGGCCGCGT GTGCAGGGAC CTGGCTGCTG CTCCGTGACCG CCCTGTGCCG GCTGGCGCGC 480  
 ACCGATCTCA CCTACCCGGT GCACGCCCTG GGCATCATCA CCTGCTTCGA CGTCCTCAAG 540  
 TGGACGATGC TCCCCAGCGT GGCCATGTGG GCCGTGTGCC TCTTCACCAT CTTCATCCTG 600  
 CTGTTCCCTCA TCCCGTTCGT GATCACCGTG GCTTGTACA CGGCCACCAT CCTCAAGCTG 660  
 TTGCGCACGG AGGAGGGCGCA CGGCCGGGAG CAGCGGAGGC GCGCGGTGGG CCTGGCCGCG 720  
 20 GTGGTCTTGC TGGCCTTGT CACCTGCTTC GCCCCAAACA ACTTCGTGCT CCTGGCGCAC 780  
 ATCGTGAGCC GCCTGTTCTA CGGCAAGAGC TACTACCACG TGTACAAGCT CACGCTGTGT 840  
 CTCAGCTGCC TCAACAACTG TCTGGACCCG TTTGTTTATT ACTTTGCGTC CCGGGAATTG 900  
 CAGCTGCGCC TGCAGGAATA TTTGGGCTGC CGCCGGGTGC CCAGAGACAC CCTGGACACG 960  
 CGCCGCGAGA GCCTCTTCTC CGCCAGGACC ACGTCCGTGC GCTCCGAGGC CGGTGCGCAC 1020  
 25 CCTGAAGGGA TGGAGGGAGC CACCAGGCC CGCCCTCCAGA GGCAGGAGAG TGTGTTCTGA 1080

(29) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 359 amino acids

- (B) TYPE: amino acid

30

- (C) STRANDEDNESS:

- (D) TOPOLOGY: not relevant

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

|    |   |  |
|----|---|--|
|    | Met Gln Val Pro Asn Ser Thr Gly Pro Asp Asn Ala Thr Leu Gln Met   |  |
|    | 1                               5   10   15                                       |  |
| 5  | Leu Arg Asn Pro Ala Ile Ala Val Ala Leu Pro Val Val Tyr Ser Leu   |  |
|    | 20   25   30                              |  |
|    | Val Ala Ala Val Ser Ile Pro Gly Asn Leu Phe Ser Leu Trp Val Leu   |  |
|    | 35    40   45                               |  |
| 10 | Cys Arg Arg Met Gly Pro Arg Ser Pro Ser Val Ile Phe Met Ile Asn   |  |
|    | 50   55   60  |  |
|    | Leu Ser Val Thr Asp Leu Met Leu Ala Ser Val Leu Pro Phe Gln Ile   |  |
|    | 65   70   75   80 |  |
|    | Tyr Tyr His Cys Asn Arg His His Trp Val Phe Gly Val Leu Leu Cys   |  |
|    | 85   90   95                                      |  |
| 15 | Asn Val Val Thr Val Ala Phe Tyr Ala Asn Met Tyr Ser Ser Ile Leu   |  |
|    | 100   105   110   |  |
|    | Thr Met Thr Cys Ile Ser Val Glu Arg Phe Leu Gly Val Leu Tyr Pro   |  |
|    | 115   120   125   |  |
| 20 | Leu Ser Ser Lys Arg Trp Arg Arg Arg Tyr Ala Val Ala Ala Cys   |  |
|    | 130   135   140   |  |
|    | Ala Gly Thr Trp Leu Leu Leu Thr Ala Leu Cys Pro Leu Ala Arg   |  |
|    | 145   150   155   160     |  |
|    | Thr Asp Leu Thr Tyr Pro Val His Ala Leu Gly Ile Ile Thr Cys Phe   |  |
|    | 165   170   175   |  |
| 25 | Asp Val Leu Lys Trp Thr Met Leu Pro Ser Val Ala Met Trp Ala Val   |  |
|    | 180   185   190   |  |
|    | Phe Leu Phe Thr Ile Phe Ile Leu Leu Phe Leu Ile Pro Phe Val Ile   |  |
|    | 195   200   205   |  |
| 30 | Thr Val Ala Cys Tyr Thr Ala Thr Ile Leu Lys Leu Leu Arg Thr Glu   |  |
|    | 210   215   220   |  |
|    | Glu Ala His Gly Arg Glu Gln Arg Arg Arg Ala Val Gly Leu Ala Ala   |  |
|    | 225   230   235   240     |  |
|    | Val Val Leu Leu Ala Phe Val Thr Cys Phe Ala Pro Asn Asn Phe Val   |  |
|    | 245   250   255   |  |
| 35 | Leu Leu Ala His Ile Val Ser Arg Leu Phe Tyr Gly Lys Ser Tyr Tyr   |  |
|    | 260   265   270   |  |

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His Val Tyr Lys Leu Thr Leu Cys Leu Ser Cys Leu Asn Asn Cys Leu  
275 280 285

Asp Pro Phe Val Tyr Tyr Phe Ala Ser Arg Glu Phe Gln Leu Arg Leu  
290 295 300

5 Arg Glu Tyr Leu Gly Cys Arg Arg Val Pro Arg Asp Thr Leu Asp Thr  
305 310 315 320

Arg Arg Glu Ser Leu Phe Ser Ala Arg Thr Thr Ser Val Arg Ser Glu  
325 330 335

0 Ala Gly Ala His Pro Glu Gly Met Glu Gly Ala Thr Arg Pro Gly Leu  
340 345 350 .

Gln Arg Gln Glu Ser Val Phe  
355

(30) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:

15                   (A) LENGTH: 1503 base pairs  
                     (B) TYPE: nucleic acid  
                     (C) STRANDEDNESS: single  
                     (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

ATGGAGCGTC CCTGGGAGGA CAGCCCAGGC CGGGAGGGGG CAGCTGAGGG CTCGCCTGTG 60  
CCAGTCGCCG CCGGGGCGCG CTCCGGTGCC GCGGCGAGTG GCACAGGCTG GCAGCCATGG 120  
GCTGAGTGCC CGGGACCCAA GGGGAGGGGG CAACTGCTGG CGACCGCCGG CCCTTGCCTG 180  
CGCTGGCCCCG CCCCCCTCGCC TGCCAGCTCC AGCCCCGCC CGGGAGCGGC GTCCGCTCAC 240  
25 TCGGTTCAAG GCAGCGCGAC TGCAGGTGGC GCACGACCAG GGCGCAGACC TTGGGGCGCG 300  
CGGCCCATGG AGTCGGGGCT GCTGCGGCCG GCGCCGGTGA GCGAGGTCAT CGTCCTGCAT 360  
TACA ACTACA CCGGCAAGCT CCGCGGTGCG AGCTACCAGC CGGGTGCCTGG CCTGCGCGCC 420  
GACGCCGTGG TGTGCCTGGC GGTGTGCGCC TTCATCGTGC TAGAGAATCT AGCCGTGTTG 480  
TTGGTGCTCG GACGCCACCC GCGCTTCCAC GCTCCCATGT TCCTCCCTCCT GGGCAGCCTC 540  
30 ACGTTGTCGG ATCTGCTGGC AGGCAGCGCC TACGCCGCCA ACATCCTACT GTCGGGGCG 600  
CTCACGCTGA AACTGTCCCC CGCGCTCTGG TTTCGCACGGG AGGCAGGGCGT CTTCGTGGCA 660  
CTCACTGCGT CCGTGCTGAG CCTCCTGCC ATCGCGCTGG AGUGCAGCCT CACCATGGCG 720

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CGCAGGGGGC CCGCGCCCGT CTCCAGTCGG GGGCGCACGC TGGCGATGGC AGCCGCGGCC 780  
 TGGGGCGTGT CGCTGCTCCT CGGGCTCCTG CCAGCGCTGG GCTGGAATTG CCTGGGTCCG 840  
 CTGGACGCTT GCTCCACTGT CTTGCCGCTC TACGCCAAGG CCTACGTGCT CTTCTGCGTG 900  
 CTCGCCTTCG TGGGCATCCT GGCCGCGATC TGTGCACTCT ACGCGCGCAT CTACTGCCAG 960  
 5 GTACGCGCCA ACGCGCGGGC CCTGCCGGCA CGGCCCGGGG CTGCGGGAC CACCTCGACC1020  
 CGGGCGCGTC GCAAGCCGCG CTCTCTGCC TTGCTGCGCA CGCTCAGCGT GGTGCTCCTG1080  
 GCCTTTGTGG CATGTTGGGG CCCCCCTCTTC CTGCTGCTGT TGCTCGACGT GGCGTGCCCG1140  
 GCGCGCACCT GTCCTGTACT CCTGCAGGCC GATCCCTTCC TGGGACTGGC CATGGCCAAC1200  
 TCACATTCTGA ACCCCATCAT CTACACGCTC ACCAACCGCG ACCTGCGCCA CGCGCTCCTG1260  
 10 CGCCTGGTCT GCTGCGGACG CCACTCCTGC GGCAGAGACC CGAGTGGCTC CCAGCAGTCG1320  
 GCGAGCGCGG CTGAGGCTTC CGGGGGCCTG CGCCGCTGCC TGCCCCCGGG CCTTGATGGG1380  
 AGCTTCAGCG GCTCGGAGCG CTCATGCC CAGCGCGACG GGCTGGACAC CAGCGGCTCC1440  
 ACAGGGCAGCC CCGGTGCACC CACAGCCGCC CGGACTCTGG TATCAGAACC GGCTGCAGAC1500  
 TGA 1503

15 (31) INFORMATION FOR SEQ ID NO:30:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 500 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS:
  - 20 (D) TOPOLOGY: not relevant
- (ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |    |    |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|
|    | Met | Glu | Arg | Pro | Trp | Glu | Asp | Ser | Pro | Gly | Pro | Glu | Gly | Ala | Ala | Glu |    |    |
|    | 1   |     |     |     |     |     |     |     |     |     |     |     |     |     | 15  |     |    |    |
| 25 | Gly | Ser | Pro | Val | Pro | Val | Ala | Ala | Gly | Ala | Arg | Ser | Gly | Ala | Ala | Ala |    |    |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 20  | 30  |    |    |
|    | Ser | Gly | Thr | Gly | Trp | Gln | Pro | Trp | Ala | Glu | Cys | Pro | Gly | Pro | Lys | Gly |    |    |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 35  | 40  | 45 |    |
| 30 | Arg | Gly | Gln | Leu | Leu | Ala | Thr | Ala | Gly | Pro | Leu | Arg | Arg | Trp | Pro | Ala |    |    |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 50  | 55  | 60 |    |
|    | Pro | Ser | Pro | Ala | Ser | Ser | Ser | Pro | Ala | Pro | Gly | Ala | Ala | Ser | Ala | His |    |    |
|    |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 65  | 70  | 75 | 80 |

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|    |   |     |     |     |
|----|---|-----|-----|-----|
|    | Ser Val Gln Gly Ser Ala Thr Ala Gly Gly Ala Arg Pro Gly Arg Arg |     |     |     |
|    | 85  | 90  | 95  |     |
|    | Pro Trp Gly Ala Arg Pro Met Glu Ser Gly Leu Leu Arg Pro Ala Pro |     |     |     |
|    | 100   | 105 | 110 |     |
| 5  | Val Ser Glu Val Ile Val Leu His Tyr Asn Tyr Thr Gly Lys Leu Arg |     |     |     |
|    | 115   | 120 | 125 |     |
|    | Gly Ala Ser Tyr Gin Pro Gly Ala Gly Leu Arg Ala Asp Ala Val Val |     |     |     |
|    | 130   | 135 | 140 |     |
| 10 | Cys Leu Ala Val Cys Ala Phe Ile Val Leu Glu Asn Leu Ala Val Leu |     |     |     |
|    | 145   | 150 | 155 | 160 |
|    | Leu Val Leu Gly Arg His Pro Arg Phe His Ala Pro Met Phe Leu Leu |     |     |     |
|    | 165   | 170 | 175 |     |
|    | Leu Gly Ser Leu Thr Leu Ser Asp Leu Leu Ala Gly Ala Ala Tyr Ala |     |     |     |
|    | 180   | 185 | 190 |     |
| 15 | Ala Asn Ile Leu Leu Ser Gly Pro Leu Thr Leu Lys Leu Ser Pro Ala |     |     |     |
|    | 195   | 200 | 205 |     |
|    | Leu Trp Phe Ala Arg Glu Gly Val Phe Val Ala Leu Thr Ala Ser     |     |     |     |
|    | 210   | 215 | 220 |     |
| 20 | Val Leu Ser Leu Leu Ala Ile Ala Leu Glu Arg Ser Leu Thr Met Ala |     |     |     |
|    | 225   | 230 | 235 | 240 |
|    | Arg Arg Gly Pro Ala Pro Val Ser Ser Arg Gly Arg Thr Leu Ala Met |     |     |     |
|    | 245   | 250 | 255 |     |
|    | Ala Ala Ala Ala Trp Gly Val Ser Leu Leu Gly Leu Leu Pro Ala     |     |     |     |
|    | 260   | 265 | 270 |     |
| 25 | Leu Gly Trp Asn Cys Leu Gly Arg Leu Asp Ala Cys Ser Thr Val Leu |     |     |     |
|    | 275   | 280 | 285 |     |
|    | Pro Leu Tyr Ala Lys Ala Tyr Val Leu Phe Cys Val Leu Ala Phe Val |     |     |     |
|    | 290   | 295 | 300 |     |
| 30 | Gly Ile Leu Ala Ala Ile Cys Ala Leu Tyr Ala Arg Ile Tyr Cys Gln |     |     |     |
|    | 305   | 310 | 315 | 320 |
|    | Val Arg Ala Asn Ala Arg Arg Leu Pro Ala Arg Pro Gly Thr Ala Gly |     |     |     |
|    | 325   | 330 | 335 |     |
|    | Thr Thr Ser Thr Arg Ala Arg Arg Lys Pro Arg Ser Leu Ala Leu Leu |     |     |     |
|    | 340   | 345 | 350 |     |
| 35 | Arg Thr Leu Ser Val Val Leu Leu Ala Phe Val Ala Cys Trp Gly Pro |     |     |     |
|    | 355   | 360 | 365 |     |
|    | Leu Phe Leu Leu Leu Leu Asp Val Ala Cys Pro Ala Arg Thr Cys     |     |     |     |

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|    |   |     |     |     |
|----|---|-----|-----|-----|
|    | 370   | 375 | 380 |     |
|    | Pro Val Leu Leu Gln Ala Asp Pro Phe Leu Gly Leu Ala Met Ala Asn |     |     |     |
|    | 385   | 390 | 395 | 400 |
| 5  | Ser Leu Leu Asn Pro Ile Ile Tyr Thr Leu Thr Asn Arg Asp Leu Arg |     |     |     |
|    | 405   | 410 | 415 |     |
|    | His Ala Leu Leu Arg Leu Val Cys Cys Gly Arg His Ser Cys Gly Arg |     |     |     |
|    | 420   | 425 | 430 |     |
|    | Asp Pro Ser Gly Ser Gln Gln Ser Ala Ser Ala Ala Glu Ala Ser Gly |     |     |     |
|    | 435   | 440 | 445 |     |
| 10 | Gly Leu Arg Arg Cys Leu Pro Pro Gly Leu Asp Gly Ser Phe Ser Gly |     |     |     |
|    | 450   | 455 | 460 |     |
|    | Ser Glu Arg Ser Ser Pro Gln Arg Asp Gly Leu Asp Thr Ser Gly Ser |     |     |     |
|    | 465   | 470 | 475 | 480 |
| 15 | Thr Gly Ser Pro Gly Ala Pro Thr Ala Ala Arg Thr Leu Val Ser Glu |     |     |     |
|    | 485   | 490 | 495 |     |
|    | Pro Ala Ala Asp   |     |     |     |
|    | 500   |     |     |     |

## (32) INFORMATION FOR SEQ ID NO:31:

- (i) SEQUENCE CHARACTERISTICS:

|    |   |
|----|---|
| 20 | <ul style="list-style-type: none"> <li>(A) LENGTH: 1029 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: single</li> <li>(D) TOPOLOGY: linear</li> </ul> |
|----|---|

(ii) MOLECULE TYPE: DNA (genomic)

## 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

```

ATGCAAGCCG TCGACAATCT CACCTCTGCG CCTGGGAACA CCAGTCTGTG CACCAGAGAC 60
TACAAAATCA CCCAGGTCTT CTTCCCCACTG CTCTACACTG TCCTGTTTT TGTTGGACTT 120
ATCACAAATG GCCTGGCGAT GAGGATTTC TTTCAAATCC GGAGTAAATC AAACCTTATT 180
ATTTTCTTA AGAACACAGT CATTCTGAT CTTCTCATGA TTCTGACTTT TCCATTCAA 240
30 ATTCTTAGTG ATGCCAAACT GGGAACAGGA CCACTGAGAA CTTTGTGTG TCAAGTTACC 300
TCCGTCATAT TTTATTCAC AATGTATATC AGTATTCAT TCCTGGGACT GATAACTATC 360
GATCGCTACC AGAAGACCAC CAGGCCATTT AAAACATCCA ACCCCAAAAAA TCTCTGGGG 420
GCTAAGATTC TCTCTGTTGT CATCTGGCA TTCATGTTCT TACTCTCTTT GCCTAACATG 480

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ATTCTGACCA ACAGGCAGCC GAGAGACAAG AATGTGAAGA AATGCTCTT CCTTAAATCA 540  
 GAGTTCGGTC TAGTCTGGCA TGAAATAGTA AATTACATCT GTCAAGTCAT TTTCTGGATT 600  
 AATTCTTAA TTGTTATTGT ATGTTATACA CTCATTACAA AAGAACTGTA CCGGTACATAC 660  
 GTAAGAACGA GGGGTGTAAG TAAAGTCCCC AGGAAAAGG TGAACGTCAA AGTTTCATT 720  
 5 ATCATTGCTG TATTCTTAT TTGTTTGTT CCTTCATT TTGCCGAAT TCCTTACACC 780  
 CTGAGCCAAA CCCGGGATGT CTTGACTGC ACTGCTGAAA ATACTCTGTT CTATGTGAAA 840  
 GAGAGCACTC TGTGGTTAAC TTCCTTAAAT GCATGCCTGG ATCCGTTCAT CTATTTTTC 900  
 CTTTGCAAGT CCTTCAGAAA TTCCTTGATA AGTATGCTGA AGTGCCCAA TTCTGCAACA 960  
 TCTCTGTCCC AGGACAATAG GAAAAAAGAA CAGGATGGTG GTGACCCAAA TGAAGAGACT1020  
 10 CCAATGTAA 1029

## (33) INFORMATION FOR SEQ ID NO:32:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 342 amino acids
  - (B) TYPE: amino acid
  - (C) STRANDEDNESS:
  - (D) TOPOLOGY: not relevant
- (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

|    |  |
|----|--|
| 20 | Met Gln Ala Val Asp Asn Leu Thr Ser Ala Pro Gly Asn Thr Ser Leu<br>1                 5                                   10                           15   |
|    | Cys Thr Arg Asp Tyr Lys Ile Thr Gln Val Leu Phe Pro Leu Leu Tyr<br>20   25                                   30                                      |
|    | Thr Val Leu Phe Phe Val Gly Leu Ile Thr Asn Gly Leu Ala Met Arg<br>35    40                                   45                                       |
| 25 | Ile Phe Phe Gln Ile Arg Ser Lys Ser Asn Phe Ile Ile Phe Leu Lys<br>50   55                                   60                                      |
|    | Asn Thr Val Ile Ser Asp Leu Leu Met Ile Leu Thr Phe Pro Phe Lys<br>65   70                                   75                                   80 |
| 30 | Ile Leu Ser Asp Ala Lys Leu Gly Thr Gly Pro Leu Arg Thr Phe Val<br>85   90                                   95                                      |
|    | Cys Gln Val Thr Ser Val Ile Phe Tyr Phe Thr Met Tyr Ile Ser Ile<br>100   105                                   110                                   |
|    | Ser Phe Leu Gly Leu Ile Thr Ile Asp Arg Tyr Gln Lys Thr Thr Arg  |

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|         |   |     |     |
|---------|---|-----|-----|
|         | 115   | 120 | 125 |
|         | Pro Phe Lys Thr Ser Asn Pro Lys Asn Leu Leu Gly Ala Lys Ile Leu |     |     |
|         | 130   | 135 | 140 |
|         | Ser Val Val Ile Trp Ala Phe Met Phe Leu Leu Ser Leu Pro Asn Met |     |     |
| 5       | 145   | 150 | 155 |
|         | Ile Leu Thr Asn Arg Gln Pro Arg Asp Lys Asn Val Lys Lys Cys Ser |     |     |
|         | 165   | 170 | 175 |
|         | Phe Leu Lys Ser Glu Phe Gly Leu Val Trp His Glu Ile Val Asn Tyr |     |     |
|         | 180   | 185 | 190 |
| 10      | Ile Cys Gln Val Ile Phe Trp Ile Asn Phe Leu Ile Val Ile Val Cys |     |     |
|         | 195   | 200 | 205 |
|         | Tyr Thr Leu Ile Thr Lys Glu Leu Tyr Arg Ser Tyr Val Arg Thr Arg |     |     |
|         | 210   | 215 | 220 |
| 15      | Gly Val Gly Lys Val Pro Arg Lys Lys Val Asn Val Lys Val Phe Ile |     |     |
|         | 225   | 230 | 235 |
|         | Ile Ile Ala Val Phe Phe Ile Cys Phe Val Pro Phe His Phe Ala Arg |     |     |
|         | 245   | 250 | 255 |
|         | Ile Pro Tyr Thr Leu Ser Gln Thr Arg Asp Val Phe Asp Cys Thr Ala |     |     |
|         | 260   | 265 | 270 |
| 20      | Glu Asn Thr Leu Phe Tyr Val Lys Glu Ser Thr Leu Trp Leu Thr Ser |     |     |
|         | 275   | 280 | 285 |
|         | Leu Asn Ala Cys Leu Asp Pro Phe Ile Tyr Phe Phe Leu Cys Lys Ser |     |     |
|         | 290   | 295 | 300 |
| 25      | Phe Arg Asn Ser Leu Ile Ser Met Leu Lys Cys Pro Asn Ser Ala Thr |     |     |
|         | 305   | 310 | 315 |
|         | Ser Leu Ser Gln Asp Asn Arg Lys Lys Glu Gln Asp Gly Gly Asp Pro |     |     |
|         | 325   | 330 | 335 |
|         | Asn Glu Glu Thr Pro Met   |     |     |
|         | 340   |     |     |
| 30 (34) | INFORMATION FOR SEQ ID NO:33:                                   |     |     |
|         | (i) SEQUENCE CHARACTERISTICS:                                   |     |     |
|         | (A) LENGTH: 1077 base pairs                                     |     |     |
|         | (B) TYPE: nucleic acid  |     |     |
|         | (C) STRANDEDNESS: single  |     |     |
| 35      | (D) TOPOLOGY: linear  |     |     |
|         | (ii) MOLECULE TYPE: DNA (genomic)                               |     |     |

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

ATGTCGGTCT GCTACCGTCC CCCAGGGAAC GAGACACTGC TGAGCTGGAA GACTTCGCGG 60  
 GCCACAGGCA CAGCCTTCCT GCTGCTGGCG GCGCTGCTGG GGCTGCCTGG CAACGGCTTC 120  
 GTGGTGTGGA GCTTGGCGGG CTGGCGGCCT GCACGGGGGC GACCGCTGGC GGCCACGCTT 180  
 5 GTGCTGCACC TGGCGCTGGC CGACGGCGCG GTGCTGCTGC TCACGCCGCT CTTTGTGGCC 240  
 TTCCCTGACCC GGCAGGCCTG GCCGCTGGGC CAGGCGGGCT GCAAGGCGGT GTACTACGTG 300  
 TGCGCGCTCA GCATGTACGC CAGCGTGCTG CTCACCGGCC TGCTCAGCCT GCAGCGCTGC 360  
 CTCGCAGTCA CCCGCCCTT CCTGGCGCCT CGGCTGCGCA GCCCGGCCCT GGCCCGCCGC 420  
 CTGCTGCTGG CGGTCTGGCT GGCCGCCCTG TTGCTCGCCG TCCC GGCCGC 480  
 10 CACCTGTGGA GGGACCGCGT ATGCCAGCTG TGCCACCCGT CGCCGGTCCA CGCCGCCGC 540  
 CACCTGAGCC TGGAGACTCT GACCGCTTTC GTGCTTCCTT TCGGGCTGAT GCTCGGCTGC 600  
 TACAGCGTGA CGCTGGCACG GCTGCGGGC GCCCGCTGGG GCTCCGGCG GCACGGGGCG 660  
 CGGGTGGGCC GGCTGGTGAG CGCCATCGTG CTTGCCTTCG 3CTTGCTCTG GGCCCGCTAC 720  
 CACGCAGTCA ACCTTCTGCA GGCGGTCGCA GCGCTGGCTC CACCGGAAGG GGCGTTGGCG 780  
 15 AAGCTGGCG GAGCCGGCCA GGCGGCGCGA GCGGGAACTA CGGCCTGGC CTTCTTCAGT 840  
 TCTAGCGTCA ACCCGGTGCT CTACGTCTTC ACCGCTGGAG ATCTGCTGCC CGGGCAGGT 900  
 CCCCCTTTCC TCACGCGGCT CTTCGAAGGC TCTGGGGAGG CCCGAGGGGG CGGCCGCTCT 960  
 AGGGAAAGGGA CCATGGAGCT CCGAACTACC CCTCAGCTGA AAGTGGTGGG GCAGGGCCGC 1020  
 GGCAATGGAG ACCCGGGGGG TGGGATGGAG AAGGACGGTC CGGAATGGGA CCTTTGA 1077

20 (35) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 358 amino acids
- (B) TYPE: amino acid

(C) STRANDEDNESS:

25 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ser | Val | Cys | Tyr | Arg | Pro | Pro | Gly | Asn | Glu | Thr | Leu | Leu | Ser | Trp |
| 1   |     |     |     |     |     |     |     |     |     |     |     |     |     |     | 15  |

30 Lys Thr Ser Arg Ala Thr Gly Thr Ala Phe Leu Leu Ala Ala Leu

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|    | 20  | 25  | 30  |
|----|---|-----|-----|
|    |   |     |     |
|    | Leu Gly Leu Pro Gly Asn Gly Phe Val Val Trp Ser Leu Ala Gly Trp |     |     |
|    | 35  | 40  | 45  |
| 5  | Arg Pro Ala Arg Gly Arg Pro Leu Ala Ala Thr Leu Val Leu His Leu |     |     |
|    | 50  | 55  | 60  |
|    | Ala Leu Ala Asp Gly Ala Val Leu Leu Leu Thr Pro Leu Phe Val Ala |     |     |
|    | 65  | 70  | 75  |
|    | Phe Leu Thr Arg Gln Ala Trp Pro Leu Gly Gln Ala Gly Cys Lys Ala |     |     |
|    | 85  | 90  | 95  |
| 10 | Val Tyr Tyr Val Cys Ala Leu Ser Met Tyr Ala Ser Val Leu Leu Thr |     |     |
|    | 100   | 105 | 110 |
|    | Gly Leu Leu Ser Leu Gln Arg Cys Leu Ala Val Thr Arg Pro Phe Leu |     |     |
|    | 115   | 120 | 125 |
| 15 | Ala Pro Arg Leu Arg Ser Pro Ala Leu Ala Arg Arg Leu Leu Leu Ala |     |     |
|    | 130   | 135 | 140 |
|    | Val Trp Leu Ala Ala Leu Leu Leu Ala Val Pro Ala Ala Val Tyr Arg |     |     |
|    | 145   | 150 | 155 |
|    | His Leu Trp Arg Asp Arg Val Cys Gln Leu Cys His Pro Ser Pro Val |     |     |
|    | 165   | 170 | 175 |
| 20 | His Ala Ala Ala His Leu Ser Leu Glu Thr Leu Thr Ala Phe Val Leu |     |     |
|    | 180   | 185 | 190 |
|    | Pro Phe Gly Leu Met Leu Gly Cys Tyr Ser Val Thr Leu Ala Arg Leu |     |     |
|    | 195   | 200 | 205 |
| 25 | Arg Gly Ala Arg Trp Gly Ser Gly Arg His Gly Ala Arg Val Gly Arg |     |     |
|    | 210   | 215 | 220 |
|    | Leu Val Ser Ala Ile Val Leu Ala Phe Gly Leu Leu Trp Ala Pro Tyr |     |     |
|    | 225   | 230 | 235 |
|    | His Ala Val Asn Leu Leu Gln Ala Val Ala Ala Leu Ala Pro Pro Glu |     |     |
|    | 245   | 250 | 255 |
| 30 | Gly Ala Leu Ala Lys Leu Gly Gly Ala Gly Gln Ala Ala Arg Ala Gly |     |     |
|    | 260   | 265 | 270 |
|    | Thr Thr Ala Leu Ala Phe Phe Ser Ser Ser Val Asn Pro Val Leu Tyr |     |     |
|    | 275   | 280 | 285 |
| 35 | Val Phe Thr Ala Gly Asp Leu Leu Pro Arg Ala Gly Pro Arg Phe Leu |     |     |
|    | 290   | 295 | 300 |
|    | Thr Arg Leu Phe Glu Gly Ser Gly Glu Ala Arg Gly Gly Gly Arg Ser |     |     |
|    | 305   | 310 | 315 |
|    |   |     | 320 |

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Arg Glu Gly Thr Met Glu Leu Arg Thr Thr Pro Gln Leu Lys Val Val  
325 330 335

Gly Gln Gly Arg Gly Asn Gly Asp Pro Gly Gly Gly Met Glu Lys Asp  
340 345 350

5 Gly Pro Glu Trp Asp Leu  
355

(36) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1005 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35.

15 ATGCTGGGGA TCATGGCATG GAATGCAACT TGCAAAACT GGCTGGCAGC AGAGGCTGCC 60  
CTGGAAAAAGT ACTACCTTTC CATTTTTAT GGGATTGAGT TCGTTGTGGG AGTCCTTGGA 120  
AATAACCATTG TTGTTTACGG CTACATCTTC TCTCTGAAGA ACTGGAACAG CAGTAATATT 180  
TATCTCTTA ACCTCTCTGT CTCTGACTTA GCTTTCTGT GCACCCCTCCC CATGCTGATA 240  
AGGAGTTATG CCAATGGAAA CTGGATATAT GGAGACGTGC TCTGCATAAG CAACCGATAT 300  
20 GTGCTTCATG CCAACCTCTA TACCAGCATT CTCTTCTCA CTTTTATCAG CATAGATCGA 360  
TACTTGATAA TTAAGTATCC TTTCCGAGAA CACCTCTGC AAAAGAAAGA GTTTGCTATT 420  
TTAACCTCCT TGGCCATTG GGTTTAGTA ACCTTAGAGT TACTACCCAT ACTTCCCCTT 480  
ATAAAATCCTG TTATAACTGA CAATGGCACC ACCTGTAATG ATTTGCAAG TTCTGGAGAC 540  
CCCAACTACA ACCTCATTG CAGCATGTGT CTAACACTGT TGGGGTTCCT TATTCCCTTT 600  
25 TTTGTGATGT GTTTCTTTA TTACAAGATT GCTCTCTTCC TAAAGCAGAG GAATAGGCAG 660  
GTTGCTACTG CTCTGCCCT TGAAAAGCCT CTCAAATTGG TCATCATGGC AGTGGTAATC 720  
TTCTCTGTGC TTTTACACC CTATCACGTC ATGCGGAATG TGAGGATCGC TTCACGCCTG 780  
GGGAGTTGGA AGCAGTATCA GTGCACTCAG GTCGTCATCA ACTCCTTTA CATTGTGACA 840  
CGGCCTTGG CCTTTCTGAA CAGTGTCAATC AACCCGTCT TCTATTCTTCTTGGGAGAT 900  
30 CACTTCAGGG ACATGCTGAT GAATCAACTG AGACACAACT TCAAATCCCT TACATCCTT 960  
AGCAGATGGG CTCATGAACCTACTTTCA TTCAGAGAAA AGTGA 1005

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(37) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 334 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

|    |  |
|----|--|
| 10 | Met Leu Gly Ile Met Ala Trp Asn Ala Thr Cys Lys Asn Trp Leu Ala<br>1 5 10 15       |
|    | Ala Glu Ala Ala Leu Glu Lys Tyr Tyr Leu Ser Ile Phe Tyr Gly Ile<br>20 25 30        |
|    | Glu Phe Val Val Gly Val Leu Gly Asn Thr Ile Val Val Tyr Gly Tyr<br>35 40 45        |
| 15 | Ile Phe Ser Leu Lys Asn Trp Asn Ser Ser Asn Ile Tyr Leu Phe Asn<br>50 55 60        |
|    | Leu Ser Val Ser Asp Leu Ala Phe Leu Cys Thr Leu Pro Met Leu Ile<br>65 70 75 80     |
| 20 | Arg Ser Tyr Ala Asn Gly Asn Trp Ile Tyr Gly Asp Val Leu Cys Ile<br>85 90 95        |
|    | Ser Asn Arg Tyr Val Leu His Ala Asn Leu Tyr Thr Ser Ile Leu Phe<br>100 105 110     |
|    | Leu Thr Phe Ile Ser Ile Asp Arg Tyr Leu Ile Ile Lys Tyr Pro Phe<br>115 120 125     |
| 25 | Arg Glu His Leu Leu Gln Lys Lys Glu Phe Ala Ile Leu Ile Ser Leu<br>130 135 140     |
|    | Ala Ile Trp Val Leu Val Thr Leu Glu Leu Leu Pro Ile Leu Pro Leu<br>145 150 155 160 |
| 30 | Ile Asn Pro Val Ile Thr Asp Asn Gly Thr Thr Cys Asn Asp Phe Ala<br>165 170 175     |
|    | Ser Ser Gly Asp Pro Asn Tyr Asn Leu Ile Tyr Ser Met Cys Leu Thr<br>180 185 190     |
|    | Leu Leu Gly Phe Leu Ile Pro Leu Phe Val Met Cys Phe Phe Tyr Tyr<br>195 200 205     |
| 35 | Lys Ile Ala Leu Phe Leu Lys Gln Arg Asn Arg Gln Val Ala Thr Ala<br>210 215 220     |

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Leu Pro Leu Glu Lys Pro Leu Asn Leu Val Ile Met Ala Val Val Ile  
 225 230 235 240

Phe Ser Val Leu Phe Thr Pro Tyr His Val Met Arg Asn Val Arg Ile  
 245 250 255

5 Ala Ser Arg Leu Gly Ser Trp Lys Gln Tyr Gln Cys Thr Gln Val Val  
 260 265 270

Ile Asn Ser Phe Tyr Ile Val Thr Arg Pro Leu Ala Phe Leu Asn Ser  
 275 280 285

10 Val Ile Asn Pro Val Phe Tyr Phe Leu Leu Gly Asp His Phe Arg Asp  
 290 295 300

Met Leu Met Asn Gln Leu Arg His Asn Phe Lys Ser Leu Thr Ser Phe  
 305 310 315 320

Ser Arg Trp Ala His Glu Leu Leu Ser Phe Arg Glu Lys  
 325 330

15 (38) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1296 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- 20 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

ATGCAGGCGC TTAACATTAC CCCGGAGCAG TTCTCTCGGC TGCTGCGGGA CCACAACCTG 60  
 ACGCGGGAGC AGTCATCGC TCTGTACCGG CTGCGACCCG TCGTCTACAC CCCAGAGCTG 120  
 25 CCGGGACGCG CCAAGCTGGC CCTCGTGCTC ACCGGCGTGC TCATCTTCGC CCTGGCGCTC 180  
 TTTGGCAATG CTCTGGTGT TCTACGTGGTG ACCCGCAGCA AGGCCATGCG CACCGTCACC 240  
 AACATTTA TCTGCTCCTT GGCGCTCAGT GACCTGCTCA TCACCTTCTT CTGCATTCCC 300  
 GTCACCATGC TCCAGAACAT TTCCGACAAC TGGCTGGGG GTGCTTCAT TTGCAAGATG 360  
 GTGCCATTG TCCAGTCTAC CGCTGTTGTG ACAGAAATGC TCACTATGAC CTGCATTGCT 420  
 30 GTGGAAAGGC ACCAGGGACT TGTGCATCCT TTTAAAATGA AGTGGCAATA CACCAACCGA 480  
 AGGGCTTC AATGCTAGG TGTGGTCTGG CTGGTGGCAG TCATCGTAGG ATCACCCATG 540  
 TGGCACGTGC AACAACTTGA GATCAAATAT GACTTCTAT ATGAAAAGGA ACACATCTGC 600  
 TGCTTACAAG AGTGGACCAG CCCTGTGCAC CAGAAGATCT ACACCCACCTT CATCCTTGTC 660

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ATCCTCTTCC TCCTGCCTCT TATGGTGATG CTTATTCTGT ACAGTAAAAT TGTTATGAA 720  
 CTTTGGATAA AGAAAAGAGT TGGGGATGGT TCAGTGCTTC GAACTATTCA TGAAAAGAA 780  
 ATGTCCAAA TAGCCAGGAA GAAGAACGA GCTGTCATTA TGATGGTGAC AGTGGTGGCT 840  
 CTCTTGCTG TGTGCTGGGC ACCATCCAT GTTGTCCATA TGATGATTGA ATACAGTAAT 900  
 5 TTTGAAAAGG AATATGATGA TGTCACAATC AAGATGATTG TTGCTATCGT GCAAATTATT 960  
 GGATTTCCA ACTCCATCTG TAATCCCATT GTCTATGCAT TTATGAATGA AAACTTCAA1020  
 AAAATGTTT TGTCTGCAGT TTGTTATTGC ATAGTAAATA AAACCTTCTC TCCAGCACAA1080  
 AGGCATGGAA ATTCAAGGAAT TACAATGATG CGGAAGAAAG CAAAGTTTC CCTCAGAGAG1140  
 AATCCAGTGG AGGAAACCAA AGGAGAAGCA TTCAGTGATG GCAACATTGA AGTCAAATTG1200  
 10 TGTGAACAGA CAGAGGAGAA GAAAAAGCTC AAACGACATC TTGCTCTCTT TAGGTCTGAA1260  
 CTGGCTGAGA ATTCTCCTTT AGACAGTGGG CATTAA 1296

## (39) INFORMATION FOR SEQ ID NO:38:

15 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 431 amino acids  
 (B) TYPE: amino acid  
 (C) STRANDEDNESS:  
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

20 Met Gln Ala Leu Asn Ile Thr Pro Glu Glr Phe Ser Arg Leu Leu Arg  
 1 5 10 15

Asp His Asn Leu Thr Arg Glu Gln Phe Ile Ala Leu Tyr Arg Leu Arg  
 20 25 30

25 Pro Leu Val Tyr Thr Pro Glu Leu Pro Gly Arg Ala Lys Leu Ala Leu  
 35 40 45

Val Leu Thr Gly Val Leu Ile Phe Ala Leu Ala Leu Phe Gly Asn Ala  
 50 55 60

Leu Val Phe Tyr Val Val Thr Arg Ser Lys Ala Met Arg Thr Val Thr  
 65 70 75 80

30 Asn Ile Phe Ile Cys Ser Leu Ala Leu Ser Asp Leu Leu Ile Thr Phe  
 85 90 95

Phe Cys Ile Pro Val Thr Met Leu Gln Asn Ile Ser Asp Asn Trp Leu

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|    |   |     |     |
|----|---|-----|-----|
|    | 100   | 105 | 110 |
|    | Gly Gly Ala Phe Ile Cys Lys Met Val Pro Phe Val Gln Ser Thr Ala |     |     |
|    | 115   | 120 | 125 |
| 5  | Val Val Thr Glu Met Leu Thr Met Thr Cys Ile Ala Val Glu Arg His |     |     |
|    | 130   | 135 | 140 |
|    | Gln Gly Leu Val His Pro Phe Lys Met Lys Trp Gln Tyr Thr Asn Arg |     |     |
|    | 145   | 150 | 155 |
|    | Arg Ala Phe Thr Met Leu Gly Val Val Trp Leu Val Ala Val Ile Val |     |     |
|    | 165   | 170 | 175 |
| 10 | Gly Ser Pro Met Trp His Val Gln Gln Leu Glu Ile Lys Tyr Asp Phe |     |     |
|    | 180   | 185 | 190 |
|    | Leu Tyr Glu Lys Glu His Ile Cys Cys Leu Glu Glu Trp Thr Ser Pro |     |     |
|    | 195   | 200 | 205 |
| 15 | Val His Gln Lys Ile Tyr Thr Thr Phe Ile Leu Val Ile Leu Phe Leu |     |     |
|    | 210   | 215 | 220 |
|    | Leu Pro Leu Met Val Met Leu Ile Leu Tyr Ser Lys Ile Gly Tyr Glu |     |     |
|    | 225   | 230 | 235 |
|    | Leu Trp Ile Lys Lys Arg Val Gly Asp Gly Ser Val Leu Arg Thr Ile |     |     |
|    | 245   | 250 | 255 |
| 20 | His Gly Lys Glu Met Ser Lys Ile Ala Arg Lys Lys Lys Arg Ala Val |     |     |
|    | 260   | 265 | 270 |
|    | Ile Met Met Val Thr Val Val Ala Leu Phe Ala Val Cys Trp Ala Pro |     |     |
|    | 275   | 280 | 285 |
| 25 | Phe His Val Val His Met Met Ile Glu Tyr Ser Asn Phe Glu Lys Glu |     |     |
|    | 290   | 295 | 300 |
|    | Tyr Asp Asp Val Thr Ile Lys Met Ile Phe Ala Ile Val Gln Ile Ile |     |     |
|    | 305   | 310 | 315 |
|    | 320   |     |     |
|    | Gly Phe Ser Asn Ser Ile Cys Asn Pro Ile Val Tyr Ala Phe Met Asn |     |     |
|    | 325   | 330 | 335 |
| 30 | Glu Asn Phe Lys Lys Asn Val Leu Ser Ala Val Cys Tyr Cys Ile Val |     |     |
|    | 340   | 345 | 350 |
|    | Asn Lys Thr Phe Ser Pro Ala Gln Arg His Gly Asn Ser Gly Ile Thr |     |     |
|    | 355   | 360 | 365 |
| 35 | Met Met Arg Lys Lys Ala Lys Phe Ser Leu Arg Glu Asn Pro Val Glu |     |     |
|    | 370   | 375 | 380 |
|    | Glu Thr Lys Gly Glu Ala Phe Ser Asp Gly Asn Ile Glu Val Lys Leu |     |     |
|    | 385   | 390 | 395 |
|    | 400   |     |     |

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Cys Glu Gln Thr Glu Glu Lys Lys Leu Lys Arg His Leu Ala Leu  
405 410 415

Phe Arg Ser Glu Leu Ala Glu Asn Ser Pro Leu Asp Ser Gly His  
420 425 430

5 (40) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

CTGTGTACAG CAGTCGCAG AGTG

24

(41) INFORMATION FOR SEQ ID NO:40:

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

GAGTGCCAGG CAGAGCAGGT AGAC

24

(42) INFORMATION FOR SEQ ID NO:41:

25 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 31 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

CCCGAATTCC TGCTTGCTCC CAGCTTGGCC C

31

(43) INFORMATION FOR SEQ ID NO:42:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 32 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
5 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

TGTGGATCCT GCTGTCAAAG GTCCCATTCC GG

32

10 (44) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 20 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
15 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

TCACAATGCT AGGTGTGGTC

20

20 (45) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
25 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

TGCATAGACA ATGGGATTAC AG

22

30 (46) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 511 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

TCACAATGCT AGGTGTGGTC TGGCTGGTGG CAGTCATCGT AGGATCACCC ATGTGGCACG 60  
5 TGCAACAACT TGAGATCAAA TATGACTTCC TATATGAAAAA GGAACACATC TGCTGCTTAG 120  
AAGAGTGGAC CAGCCCTGTG CACCAGAAGA TCTACACCAC CTTCATCCTT GTCATCCTCT 180  
TCCTCCTGCC TCTTATGGTG ATGCTTATTG TGTACGTAAA ATTGGTTATG AACTTTGGAT 240  
AAAGAAAAGA GTTGGGGATG GTTCAGTGCT TCGAACTATT CATGGAAAAG AAATGTCCAA 300  
AATAGCCAGG AAGAAGAAC GAGCTGTCAT TATGATGGTG ACAGTGGTGG CTCTCTTGC 360  
10 TGTGTGCTGG GCACCATTCC ATGTTGTCCA TATGATGATT GAATACAGTA ATTTTGAAAAA 420  
GGAATATGAT GATGTCACAA TCAAGATGAT TTTTGTATC GTGCAAATTA TTGGATTTTC 480  
CAACTCCATC TGTAATCCCA TTGTCTATGC A 511

(47) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

CTGCTTAGAA GAGTGGACCA G

21

(48) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30 (iv) ANTI-SENSE: NO

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

CTGTGCACCA GAAGATCTAC AC

22

(49) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

CAAGGATGAA GGTGGTGTAG A

21

(50) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

GTGTAGATCT TCTGGTGCAC AGG

23

(51) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 21 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

GCAATGCAGG TCATAGTGAG C

21

(52) INFORMATION FOR SEQ ID NO:51:

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(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 27 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
5 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

10 TGGAGCATGG TGACGGGAAT GCAGAAAG

27

(53) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 27 base pairs  
(B) TYPE: nucleic acid  
15 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

20 GTGATGAGCA GGTCACTGAG CGCCAAG

27

(54) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 23 base pairs  
(B) TYPE: nucleic acid  
25 (C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

30 GCAATGCAGG CGCTTAACAT TAC

23

(55) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 22 base pairs

- 54 -

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

5 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

TTGGGTTACA ATCTGAAGGG CA

22

(56) INFORMATION FOR SEQ ID NO:55:

- (i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

15 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

ACTCCGTGTC CAGCAGGACT CTG

23

(57) INFORMATION FOR SEQ ID NO:56:

- (i) SEQUENCE CHARACTERISTICS:

- 20 (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

25 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

TGCGTGTTC TGGACCCCTCA CGTG

24

(58) INFORMATION FOR SEQ ID NO:57:

- (i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 29 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

CAGGCCTTGG ATTTTAATGT CAGGGATGG

29

5 (59) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- 10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

GGAGAGTCAG CTCTGAAAGA ATTCAAGG

27

15 (60) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- 20 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

TGATGTGATG CCAGATACTA ATAGCAC

27

25 (61) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- 30 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

CCTGATTCA TTAGGTGAGA TTGAGAC

27

(62) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

GACAGGTACC TTGCCATCAA G

21

(63) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 22 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

CTGCACAATG CCAGTGATAA GG

22

(64) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 27 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

CTGACTTCTT GTTCCTGGCA GCAGCGG

27

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## (65) INFORMATION FOR SEQ ID NO:64:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 27 base pairs
- (B) TYPE: nucleic acid
- 5 (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

10 AGACCAGCCA GGGCACGCTG AAGAGTG

27

## (66) INFORMATION FOR SEQ ID NO:65:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 32 base pairs
- (B) TYPE: nucleic acid
- 15 (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

20 GATCAAGCTT CCATCCTACT GAAACCATGG TC

32

## (67) INFORMATION FOR SEQ ID NO:66:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 35 base pairs
- (B) TYPE: nucleic acid
- 25 (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

30 GATCAGATCT CAGTTCCAAT ATTACACCCA CCGTC

35

## (68) INFORMATION FOR SEQ ID NO:67:

## (i) SEQUENCE CHARACTERISTICS:

- 58 -

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

CTGGTGTGCT CCATGGCATC CC

22

(69) INFORMATION FOR SEQ ID NO:68:

10 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

GTAAGCCTCC CAGAACGAGA GG

22

(70) INFORMATION FOR SEQ ID NO:69:

20 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

CAGCGCAGGG TGAAGCCTGA GAGC

24

(71) INFORMATION FOR SEQ ID NO:70:

30 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- 59 -

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

GGCACCTGCT GTGACCTGTG CAGG

24

5 (72) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

10 (ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

GTCCTGCCAC TTCGAGACAT GG

22

15 (73) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 23 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

GAAACTTCTC TGCCCTTACC GTC

23

25 (74) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

CCAACACCAAG CATCCATGGC ATCAAAG

26

(75) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:

5           (A) LENGTH: 27 base pairs  
              (B) TYPE: nucleic acid  
              (C) STRANDEDNESS: single  
              (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10          (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

GGAGAGTCAG CTCTGAAAGA ATTCAAGG

27



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|   |                              |            |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
|---|------------------------------|------------|--|----|------------|-----------------------------|----|------------|-----------------------------|----|------------|--------------------------|----|------------|--------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|------------------------|----|------------|-------------------------|----|------------|------------------------------|----|------------|------------------------------|----|------------|------------------------------|----|------------|------------------------------|----|------------|---------------------------|----|------------|---------------------------|----|------------|---------------------------|----|------------|---------------------------|----|------------|---------------------------|----|------------|----------------------------|----|------------|----------------------------|----|--|
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| <p>(21) International Application Number: PCT/US99/23687</p> <p>(22) International Filing Date: 13 October 1999 (13.10.99)</p> <p>(30) Priority Data:</p> <table> <tbody> <tr><td>60/109,213</td><td>20 November 1998 (20.11.98)</td><td>US</td></tr> <tr><td>60/120,416</td><td>16 February 1999 (16.02.99)</td><td>US</td></tr> <tr><td>60/121,852</td><td>26 February 1999 (26.02.99)</td><td>US</td></tr> <tr><td>60/123,946</td><td>12 March 1999 (12.03.99)</td><td>US</td></tr> <tr><td>60/123,949</td><td>12 March 1999 (12.03.99)</td><td>US</td></tr> <tr><td>60/136,436</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/136,437</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/136,439</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/136,567</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/137,127</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/137,131</td><td>28 May 1999 (28.05.99)</td><td>US</td></tr> <tr><td>60/141,448</td><td>29 June 1999 (29.06.99)</td><td>US</td></tr> <tr><td>60/156,653</td><td>29 September 1999 (29.09.99)</td><td>US</td></tr> <tr><td>60/156,633</td><td>29 September 1999 (29.09.99)</td><td>US</td></tr> <tr><td>60/156,555</td><td>29 September 1999 (29.09.99)</td><td>US</td></tr> <tr><td>60/156,634</td><td>29 September 1999 (29.09.99)</td><td>US</td></tr> <tr><td>60/157,280</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>60/157,294</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>60/157,281</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>60/157,293</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>60/157,282</td><td>1 October 1999 (01.10.99)</td><td>US</td></tr> <tr><td>09/417,044</td><td>12 October 1999 (12.10.99)</td><td>US</td></tr> <tr><td>09/416,760</td><td>12 October 1999 (12.10.99)</td><td>US</td></tr> </tbody> </table> |                              | 60/109,213 | 20 November 1998 (20.11.98)  | US | 60/120,416 | 16 February 1999 (16.02.99) | US | 60/121,852 | 26 February 1999 (26.02.99) | US | 60/123,946 | 12 March 1999 (12.03.99) | US | 60/123,949 | 12 March 1999 (12.03.99) | US | 60/136,436 | 28 May 1999 (28.05.99) | US | 60/136,437 | 28 May 1999 (28.05.99) | US | 60/136,439 | 28 May 1999 (28.05.99) | US | 60/136,567 | 28 May 1999 (28.05.99) | US | 60/137,127 | 28 May 1999 (28.05.99) | US | 60/137,131 | 28 May 1999 (28.05.99) | US | 60/141,448 | 29 June 1999 (29.06.99) | US | 60/156,653 | 29 September 1999 (29.09.99) | US | 60/156,633 | 29 September 1999 (29.09.99) | US | 60/156,555 | 29 September 1999 (29.09.99) | US | 60/156,634 | 29 September 1999 (29.09.99) | US | 60/157,280 | 1 October 1999 (01.10.99) | US | 60/157,294 | 1 October 1999 (01.10.99) | US | 60/157,281 | 1 October 1999 (01.10.99) | US | 60/157,293 | 1 October 1999 (01.10.99) | US | 60/157,282 | 1 October 1999 (01.10.99) | US | 09/417,044 | 12 October 1999 (12.10.99) | US | 09/416,760 | 12 October 1999 (12.10.99) | US | (71) Applicant (for all designated States except US): ARENA PHARMACEUTICALS, INC. [US/US]; 6166 Nancy Ridge Drive, San Diego, CA 92121 (US). |
| 60/109,213  | 20 November 1998 (20.11.98)  | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
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| 60/136,439  | 28 May 1999 (28.05.99)       | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/136,567  | 28 May 1999 (28.05.99)       | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/137,127  | 28 May 1999 (28.05.99)       | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/137,131  | 28 May 1999 (28.05.99)       | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/141,448  | 29 June 1999 (29.06.99)      | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/156,653  | 29 September 1999 (29.09.99) | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/156,633  | 29 September 1999 (29.09.99) | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/156,555  | 29 September 1999 (29.09.99) | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/156,634  | 29 September 1999 (29.09.99) | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/157,280  | 1 October 1999 (01.10.99)    | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/157,294  | 1 October 1999 (01.10.99)    | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/157,281  | 1 October 1999 (01.10.99)    | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/157,293  | 1 October 1999 (01.10.99)    | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 60/157,282  | 1 October 1999 (01.10.99)    | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 09/417,044  | 12 October 1999 (12.10.99)   | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
| 09/416,760  | 12 October 1999 (12.10.99)   | US         |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
|   |                              |            | (72) Inventors: and<br>(75) Inventors/Applicants (for US only): CHEN, Ruoping [CN/US]; 5296 Timber Branch Way, San Diego, CA 92130 (US). DANG, Huong, T. [US/US]; 5352 Oak Park Drive, San Diego, CA 92105 (US). LIAW, Chen, W. [US/US]; 7668 Salix Place, San Diego, CA 92129 (US). LIN, I-Lin [-US]; 8291-7 Gold Coast Drive, San Diego, CA 92126 (US).  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
|   |                              |            | (74) Agents: MILLER, Suzanne, E. et al.; Woodcock Washburn Kurtz Mackiewicz & Norris LLP, 46th floor, One Liberty Place, Philadelphia, PA 19103 (US).  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |
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| <p>(54) Title: HUMAN ORPHAN G PROTEIN-COUPLED RECEPTORS</p> <p>(57) Abstract</p> <p>The invention disclosed in this patent document relates to transmembrane receptors, more particularly to endogenous, human orphan G protein-coupled receptors.</p>  |                              |            |  |    |            |                             |    |            |                             |    |            |                          |    |            |                          |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                        |    |            |                         |    |            |                              |    |            |                              |    |            |                              |    |            |                              |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                           |    |            |                            |    |            |                            |    |  |

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| DE | Germany                  | LK | Sri Lanka                             | SE | Sweden                                    |    |                          |
| DK | Denmark                  | LR | Liberia                               | SG | Singapore                                 |    |                          |
| EE | Estonia                  |    |                                       |    |   |    |                          |

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 99/23687

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 C12N15/12 C07K14/72

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

14 July 2000

Date of mailing of the international search report

02.08.00

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
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Authorized officer

Mandl, B

**INTERNATIONAL SEARCH REPORT**

|                 |                       |
|-----------------|-----------------------|
| Inte            | .ional Application No |
| PCT/US 99/23687 |                       |

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT |   |                           |
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| Inte            | .ional Application No |
| PCT/US 99/23687 |                       |

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

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## INTERNATIONAL SEARCH REPORT

Inte. onal Application No  
PCT/US 99/23687

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT |  |                       |
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| E  | WO 00 12707 A (MILLENNIUM PHARM INC)<br>9 March 2000 (2000-03-09)<br>the whole document<br>---   | 49-52                 |
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## INTERNATIONAL SEARCH REPORT

Inte  
onal Application No  
PCT/US 99/23687

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT |  |                       |
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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 99/23687

### Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-4

Human G protein-coupled receptor as characterized by SEQ.ID.2, a cDNA encoding said receptor as characterized by SEQ.ID.1, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

2. Claims: 5-8

Human G protein-coupled receptor as characterized by SEQ.ID.4, a cDNA encoding said receptor as characterized by SEQ.ID.3, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

3. Claims: 9-12

Human G protein-coupled receptor as characterized by SEQ.ID.6, a cDNA encoding said receptor as characterized by SEQ.ID.5, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

4. Claims: 13-16

Human G protein-coupled receptor as characterized by SEQ.ID.8, a cDNA encoding said receptor as characterized by SEQ.ID.7, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

5. Claims: 17-20

Human G protein-coupled receptor as characterized by SEQ.ID.10, a cDNA encoding said receptor as characterized by SEQ.ID.9, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

6. Claims: 21-24

Human G protein-coupled receptor as characterized by SEQ.ID.12, a cDNA encoding said receptor as characterized by SEQ.ID.11, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

7. Claims: 25-28

Human G protein-coupled receptor as characterized by SEQ.ID.14, a cDNA encoding said receptor as characterized by

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

SEQ.ID.13, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

8. Claims: 29-32

Human G protein-coupled receptor as characterized by SEQ.ID.16, a cDNA encoding said receptor as characterized by SEQ.ID.15, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

9. Claims: 33-36

Human G protein-coupled receptor as characterized by SEQ.ID.18, a cDNA encoding said receptor as characterized by SEQ.ID.17, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

10. Claims: 37-40

Human G protein-coupled receptor as characterized by SEQ.ID.20, a cDNA encoding said receptor as characterized by SEQ.ID.19, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

11. Claims: 41-44

Human G protein-coupled receptor as characterized by SEQ.ID.22, a cDNA encoding said receptor as characterized by SEQ.ID.21, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

12. Claims: 45-48

Human G protein-coupled receptor as characterized by SEQ.ID.24, a cDNA encoding said receptor as characterized by SEQ.ID.23, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

13. Claims: 49-52

Human G protein-coupled receptor as characterized by SEQ.ID.26, a cDNA encoding said receptor as characterized by SEQ.ID.25, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

14. Claims: 53-56

Human G protein-coupled receptor as characterized by

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

SEQ.ID.28, a cDNA encoding said receptor as characterized by SEQ.ID.27, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

15. Claims: 57-60

Human G protein-coupled receptor as characterized by SEQ.ID.30, a cDNA encoding said receptor as characterized by SEQ.ID.29, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

16. Claims: 61-64

Human G protein-coupled receptor as characterized by SEQ.ID.32, a cDNA encoding said receptor as characterized by SEQ.ID.31, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

17. Claims: 65-68

Human G protein-coupled receptor as characterized by SEQ.ID.34, a cDNA encoding said receptor as characterized by SEQ.ID.33, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

18. Claims: 69-72

Human G protein-coupled receptor as characterized by SEQ.ID.36, a cDNA encoding said receptor as characterized by SEQ.ID.35, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

19. Claims: 73-76

Human G protein-coupled receptor as characterized by SEQ.ID.38, a cDNA encoding said receptor as characterized by SEQ.ID.37, a plasmid comprising said cDNA, and a host cell comprising said plasmid.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

|       |                 |
|-------|-----------------|
| Int'l | Application No  |
|       | PCT/US 99/23687 |

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